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United States Senate
HEALTH, EDUCATION, LABOR, AND PENSIONS COMMITTEE
Patty Murray, Ranking Member

**Preventable Tragedies:
Superbugs and How Ineffective Monitoring of
Medical Device Safety Fails Patients**

Minority Staff Report

January 13, 2016

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Executive Summary

In September 2013, staff at Virginia Mason Hospital and Medical Center in Seattle, Washington, traced a cluster of antibiotic-resistant infections in patients to a medical device called a closed-channel duodenoscope, which is used to identify and treat conditions of the pancreas and bile duct. Around the same time, staff at Advocate Lutheran General Hospital outside of Chicago, with the help of the Centers for Disease Control and Prevention, similarly linked an outbreak of superbug infections to closed-channel duodenoscopes.

- Both hospitals concluded that closed-channel duodenoscopes remained contaminated even after proper cleaning, spreading bacteria between patients, but it took 17 more months for duodenoscope manufacturers and the Food and Drug Administration (FDA) to alert hospitals, doctors, and the public to the risk posed by the devices.
- In January 2015, after several outbreaks of serious infections, including in Seattle, became public, Senator Patty Murray, the Ranking Member of the Senate Health, Education, Labor, and Pensions Committee, initiated an investigation to determine the extent of duodenoscope-linked infections, understand the slow response, and determine if legislative changes were needed to prevent similar problems in the future.
- Senator Murray's staff investigation has demonstrated that the clusters of infections at Virginia Mason and Advocate Lutheran were not isolated incidents. Between 2012 and spring 2015, closed-channel duodenoscopes were linked to at least 25 different incidents of antibiotic-resistant infections that sickened at least 250 patients worldwide.
- The investigation found that by early 2013, Olympus, the manufacturer of 85 percent of the duodenoscopes used in the United States, knew of two independent lab reports finding that the closed-channel model duodenoscope could harbor and spread bacteria even after cleaning according to the manufacturer's instructions. Olympus never brought this information to FDA, and did not alert hospitals, physicians or patients in the U.S. to the risk of infection until February 2015.
- The investigation also found that Olympus, as well as the other two manufacturers of duodenoscopes used in the United States, Pentax and Fujifilm, and Custom Ultrasonics, the manufacturer of the automated cleaning machine in use at many of the hospitals that experienced infections, failed to meet the obligations placed upon them by the current regulatory system. Two of the manufacturers failed to seek FDA clearance before selling the "closed-channel" duodenoscopes, all failed to adequately test whether the scopes could be cleaned reliably in real-world settings, and fully comply with adverse events reporting

requirements.

- Additionally, although at least 16 separate U.S. hospitals traced antibiotic-resistant infections directly to duodenoscopes, the hospitals generally did not raise alarms about these infections with federal regulators. It appears that not a single hospital that experienced infection outbreaks tied to the duodenoscopes sent the required adverse event form to the device manufacturers.
- When hospitals did take required action to report adverse events to device manufacturers it was often late, notification was made informally by phone or email, and reports were not

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inclusive of all the information necessary for the manufacturers to themselves submit accurate and complete information to FDA.

- While FDA started investigating how closed-channel duodenoscopes cleaned according to manufacturers' instructions spread infection in September of 2013, the agency took no action to alert hospitals, doctors and the public to the risk posed by closed-channel duodenoscopes for 17 months. At least 68 patients in seven different hospitals in the United States were infected with antibiotic-resistant bacteria linked to duodenoscopes during this period.
- Problems with FDA's outmoded adverse event device database, as well as slow and incomplete reporting by manufacturers and hospitals, appear to have left FDA staff unable to develop an accurate sense of the frequency and severity of the infection outbreaks. FDA was also unaware that by early 2013, two independent labs in Europe had documented the Olympus closed channel duodenoscope remaining contaminated after repeated cleaning, or that a Dutch Health Ministry report in 2013 had already concluded that Olympus did not have the data to show their cleaning instructions worked consistently and effectively.
- As a result, the FDA wasted valuable time seeking cleaning data from manufacturers and trying to conclusively determine that cleaning mistakes by hospital staff in cleaning were not the responsible for the infections. Unlike FDA's surveillance of drugs, where the agency is increasingly able to use the "Sentinel" system to develop fast and accurate information about adverse events, FDA had no way to seek independent information about adverse events linked to medical devices.
- The failure of FDA's current device safety reporting system to rapidly identify duodenoscope-related, antibiotic-resistant infections, including superbug infections, should serve as warning that without a comprehensive postmarket device surveillance system that supplements self-reporting from hospitals and manufacturers, future device issues are likely to go undetected for far too long and with life-threatening consequences.
- To minimize future delays in identifying and addressing device safety issues, the report recommends:
 - o Congress require unique device identifiers (UDIs) to be included in insurance claims and fully fund a National Medical Device Evaluation System to ensure that FDA is able to effectively monitor the safety of medical devices on the market rather than relying on adverse event reporting.
 - o FDA quickly evaluate the design of closed-channel duodenoscopes and implement a phased recall to fix or modify the devices if necessary.

- o FDA update its guidance to clarify when manufacturers are required to seek 510(k) clearance when medical devices are modified, and that Congress clarify FDA's authority to consider a 510(k) application incomplete in the absence of sufficient data to demonstrate a medical device can be safely cleaned and reused.
- o FDA implement new draft guidance to more quickly disseminate information to health care providers when the agency becomes aware of information that patient safety might be compromised by a medical device; and
- o Compliance by hospitals with adverse event reporting related to medical devices be made a Condition of Participation in Medicare.

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Introduction

In the summer of 2013, staff at Virginia Mason Hospital in Seattle, Washington realized that multiple patients were contracting the same type of antibiotic-resistant infection after undergoing a specific procedure at the hospital. By September 2013, after conducting an extensive epidemiological investigation in conjunction with the King County and Washington State Health Departments, the hospital linked the infections to closed-channel duodenoscopes. Duodenoscopes are medical devices used in a procedure called endoscopic retrograde cholangiopancreatography (ERCP) to diagnose and treat problems in the bile or pancreatic ducts. By the time the hospital successfully contained the outbreak of infections in early 2014, at least 32 patients at Virginia Mason were infected with antibiotic-resistant infections after undergoing ERCP.¹ At least eleven of those patients later died, although it is unclear whether those deaths were a direct result of the infections.²

During the same period in 2013 when patients at Virginia Mason were falling ill, 32 patients contracted carbapenem-resistant Enterobacteriaceae (CRE), a bacteria that is resistant to even the most potent antibiotics, after undergoing ERCP at Advocate Lutheran General Hospital in Park Ridge, Illinois. CRE is a deadly bacteria, often called a “superbug,” that kills almost half of those infected. The Centers for Disease Control and Prevention (CDC) investigated the outbreak after Advocate Lutheran requested assistance with identifying the source of the bacteria and containing the infection. By September 2013, CDC and Advocate Lutheran had determined that the CRE outbreak in Illinois – like the outbreak in Washington – was linked to ERCP procedures using closed-channel duodenoscopes.

After *The Seattle Times* broke the news in late January 2015 that Virginia Mason had experienced an outbreak of antibiotic-resistant infections in ERCP patients, Senator Patty Murray, Ranking Member of the Senate Committee on Health, Education, Labor, and Pensions (HELP), initiated an investigation into these dangerous duodenoscope-linked infections. In February and March 2015, Senator Murray sent two letters to the Food and Drug Administration (FDA), and in June she sent requests for documents to the three manufacturers of closed-channel duodenoscopes sold in the United States: Olympus Medical Systems (Olympus), Hoya Corporation PENTAX Life Care Division (Pentax), and Fujifilm Medical Systems (Fujifilm). All three manufacturers provided significant information in response to the request, including previously unavailable independent reports provided by Olympus. Senator Murray's staff also conducted interviews with hospitals, subject matter experts, independent investigators, state and local health departments, CDC, and

FDA.

Senator Murray's staff investigation has demonstrated that the clusters of infections at Virginia Mason and Advocate Lutheran linked to closed-channel duodenoscopes were not isolated incidents. Between 2012 and spring of 2015, the Olympus closed-channel duodenoscope used at Virginia Mason, together with closed-channel models made by Pentax and Fujifilm, were linked to at least 25 different instances of antibiotic-resistant infections that sickened at least 250 patients worldwide. Because some of the identified infections had unique markers that made the

Between 2012 and spring 2015, closed-channel duodenoscopes were linked to at least 25 different instances of antibiotic-resistant infections that sickened at least 250 patients worldwide.

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bacteria possible to track, and because the hospitals that have reported infections are primarily large research hospitals and medical centers adept at spotting and addressing antibiotic-resistant infections, it is likely that there are more incidents of infections linked to these devices that have never been identified.

The investigation found that Olympus, the manufacturer of 85 percent of the duodenoscopes used in the United States, knew by May 2012 that the closed-channel duodenoscope model used at Virginia Mason could harbor and spread bacteria even after proper cleaning. By the fall of 2012, Olympus was aware that its duodenoscopes had been linked to antibiotic-resistant infections, including superbug infections, caused by life-threatening multidrug-resistant organisms at hospitals in both the United States and Europe. By early 2013, independent laboratory tests of at least two different closed-channel duodenoscopes showed the devices remained contaminated after careful repeated cleaning and reprocessing.

Despite this, Olympus issued no safety alerts or guidance to hospitals and physicians in the United States until February 2015 – almost three years after first realizing the problem in April 2012. In contrast, Olympus sent some hospitals in Europe two separate alerts in 2013 and 2014, which, at the very least, advised extra caution when cleaning these duodenoscopes.

Olympus, Fujifilm, and Pentax also failed to meet their obligations to provide FDA with the

At the time duodenoscope manufacturers sold their devices to hospitals in the United States, they lacked sufficient data to show their cleaning instructions worked. to reliably decontaminate the

uses. Finally, the manufacturers did not consistently report the information they had regarding infections linked to the devices.

information the agency needs to keep patients safe.

Olympus and Fujifilm never applied for FDA clearance for the new design of the closed-channel duodenoscope before selling the devices in the United States. The manufacturers also attested to FDA that they had tested their duodenoscope cleaning instructions and demonstrated that they worked reliably. However, none of the manufacturers actually had sufficient data to show that duodenoscopes could be reliably cleaned between

Additionally, the investigation found that many, although not all, of the domestic hospitals with duodenoscope-linked outbreaks used an automated endoscope reprocessor (AER) manufactured by Custom Ultrasonics. Custom Ultrasonics, like the duodenoscope manufacturers, failed to meet its regulatory obligations, including filing appropriate applications with FDA, testing its machines

sufficiently to make sure they worked, and filing complete and accurate adverse event reports. In November 2015, FDA issued a mandatory recall of all Custom Ultrasonics AERs.

Further, the investigation established that although at least 16 separate domestic hospitals traced antibiotic-resistant infections directly to ERCP procedures, as a group, the facilities generally failed to quickly raise alarms with FDA and CDC. In some cases, hospitals completely failed to make the required reports of infections to the devices' manufacturers. This limited and slow reporting by hospitals likely impaired FDA's ability to accurately assess the frequency and severity of outbreaks of duodenoscopy-linked infections.

Failures by device manufacturers and hospitals to quickly and completely disclose important information to FDA, and FDA's outmoded adverse event system, hampered the agency's ability to accurately assess and respond to the infections. Because FDA did not have prompt and complete

information, it took the agency overly long to accept that duodenoscopy-linked infections were not the result of hospital cleaning errors. As a result, contaminated duodenoscopes spread serious infections for at least three years before manufacturers and FDA alerted hospitals in the United States. FDA's first safety communication regarding duodenoscopy cleaning did not occur for almost 17 months after the agency first became aware of the spread of infections. In the interim, at least 68 patients were affected in seven different hospitals in the United States.

Between the time FDA learned duodenoscopes could remain contaminated even after proper cleaning and the first safety alerts, at least 68 patients in seven different hospitals in the United States were infected with antibiotic-resistant infections.

The investigation provides a vivid example of the failure of FDA's current system for tracking and monitoring the safety of medical devices on the market (the postmarket surveillance system). FDA's postmarket surveillance system relies too heavily on self-reporting from manufacturers and hospitals with competing priorities that weigh against full and fast disclosure of patient safety concerns. This passive postmarket surveillance system inhibits FDA's ability to quickly identify information related patient health and device safety. Until a system is implemented that allows FDA to independently monitor, track, and assess the performance of devices, the agency will not be able to adequately identify risks to patient safety from particular devices like duodenoscopes and move quickly to address those risks.

Many Hospitals Experienced Infections Linked to Closed-Channel Duodenoscopes

Senator Murray's staff investigation has revealed that outbreaks of antibiotic-resistant infections caused by deadly multidrug-resistant organisms spread by duodenoscopes were vastly more widespread than previously reported. In June 2015, when Senator Murray first sought information from Olympus, Pentax, and Fujifilm, the three manufacturers of duodenoscopes sold in the United States, the Food and Drug Administration (FDA) had recently announced that there had been at least nine outbreaks of infections related to duodenoscopes.³ According to documents provided to the Health, Education, Labor, and Pensions (HELP) Committee, however, from 2012 through

spring of 2015, there have actually been at least 25 separate outbreaks of patient infections following endoscopic retrograde cholangiopancreatography (ERCP) procedures with closed-channel scopes in four different countries and 10 states. These outbreaks infected at least 250 people with life-threatening illnesses including carbapenem-resistant Enterobacteriaceae (CRE), a dangerous superbug that is resistant to our most potent antibiotics and that kills about half of those it infects.⁴

Institutions where antibiotic-resistant infections linked to duodenoscopes occurred include:¹

¹ The number of patients infected and date of infections indicate committee staffs' understanding based on the totality of the information obtained during this investigation. They are estimates only.

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Hospital	Estimated # of Patients Infected	Approximate time infections	Duodenoscope Manufacturer
Erasmus Medical Center, Rotterdam, Netherlands	30	January 2012	Olympus
Clinique De Bercy, Charenton-le-Pont, France	3	October 2012	Olympus
University of Pittsburgh Medical Center Presbyterian Hospital, Pittsburgh, PA	13s	November 2012	Olympus
New York-Presbyterian/Weill Cornell Medical Center, New York City, NY	15	December 2012	Olympus
UMass Memorial Medical Center, Worcester, MA	20	December 2012	Olympus
Carolinas Medical Center, Charlotte, NC	1	2013	Olympus
Thomas Jefferson University Hospital, Philadelphia, PA	8	January 2013	Olympus
Charite-Universitätsmedizin, Berlin, Germany	5	February 2013	Olympus
Advocate Lutheran General Hospital, Park Ridge, IL	32	March 2013	Pentax
Froedtert Hospital, Milwaukee, WI	5	May 2013	Olympus
Virginia Mason Hospital and Medical Center, Seattle, WA	32	Spring/Summer 2013	Olympus
Clinique De Bercy, Charenton-Le-Pont, France	2	November 2013	Olympus
Hartford Hospital, Hartford, CT	12	January 2014	Olympus
Massachusetts General Hospital,	7	Before Spring 2014	Pentax

Boston, MA Advocate Good Samaritan Hospital, Downers Grove, IL	3	May 2014	Fujifilm
Evangelisches Waldkrankenhaus, Spandau, Berlin, Germany	4	May 2014	Olympus
Boca Raton Regional Hospital, Boca Raton, FL	9%	August 2014	Olympus
Cedars-Sinai Medical Center, Torrance, CA	4	August 2014	Olympus
UCLA Medical Center, Los Angeles, CA	7	October 2014	Olympus

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Carolinas Medical Center, Charlotte, NC	18	2015	Olympus
MGH Gastroenterology Associates, Boston, MA	5	January 2015	Pentax
Massachusetts General Hospital, Boston, MA	3	January 2015	Pentax
Universitair Medisch Centrum, Utrecht, Netherlands	8	January 2015	Olympus
Allegheny General Hospital, Pittsburgh, PA	1	February 2015	Olympus
Fox Chase Cancer Center, Philadelphia, PA	3	April 2015	Fujifilm

Because some of the infections identified had unique markers that made the bacteria possible to track, and because the hospitals that have reported infections are primarily large, well-resourced research hospitals adept at spotting and addressing antibiotic-resistant infections, it is likely that there have been more incidents of infections linked to these devices that were never identified.

Background

Duodenoscopes, Reprocessing, and Automated Endoscope Reprocessors

Duodenoscopes are flexible, hollow tubes that are typically used during ERCP to treat patients suffering from blockage in their bile or pancreatic ducts due to tumors and other serious medical conditions.⁷ Doctors in the United States performed more than 660,000 potentially lifesaving ERCP procedures in 2014.⁸ Duodenoscopes are currently sold in the United States by three companies based in Japan: Olympus, Fujifilm, and Pentax. Olympus manufactures about 85 percent of the duodenoscopes used in the United States, Pentax about 12 percent, and Fujifilm only about three percent.⁹

All types of endoscopes can spread infection by passing bodily fluids or debris from one patient to subsequent patients if they are

not properly cleaned between uses. Careful cleaning is especially critical for duodenoscopes because they are used in parts of the body with high levels of bacteria and patients undergoing procedures with duodenoscopes are often already very ill, raising the risk of infection. Also, a duodenoscope's elevator channel, which allows physicians to insert a guidewire and catheter into the duodenum, is particularly difficult to clean between uses. In early duodenoscopes, the elevator wire channel was open and exposed to bodily fluids, while the newer "closed-channel" duodenoscope model seals off the elevator wire channel from contaminants.¹⁰

Picture taken from www.olympus.co.uk

To ensure that a duodenoscope does not spread infection, it must undergo reprocessing, a multi-step cleaning procedure to ensure the device is safe for re-use.¹¹ There are generally three steps to duodenoscope reprocessing:

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- 1) Point-of-use Processing: Hospitals perform point-of-use processing immediately after a device has been used by rinsing or wiping the device to make sure that contaminants do not dry and make cleaning more difficult.¹²
- 2) Thorough Cleaning: After point-of-use processing, a technician uses a brush to ensure all parts of the device are cleansed of any soil and debris. Thorough cleaning is essential because debris and other material remaining on a duodenoscope can interfere with the final disinfection or sterilization phase of reprocessing.¹³
- 3) High Level Disinfection: Devices like duodenoscopes that contact mucous membranes or non-intact skin, but that cannot withstand heat sterilization, are required to undergo high level disinfection (HLD), which kills most microbes remaining after thorough cleaning.¹⁴ Most hospitals achieve HLD by using an AER. AERs flush liquid chemicals through the scope to destroy lingering contamination after cleaning and then rinse the scope to remove the chemical before reuse.¹⁵

FDA's Regulation of Devices

FDA oversees the safety and effectiveness medical devices, more than 1,700 of which are classified by the agency into three different categories based on the amount of risk they pose to patient health and safety.¹⁶ Duodenoscopes are classified as Class II devices, which pose a medium level of risk.¹⁷ When a manufacturer modifies the design of a Class II device in a way that might implicate the safety or effectiveness of that device, it must make what is known as a "510(k) submission" to show FDA that the device remains "substantially equivalent" to a device the agency has already cleared and that the design change does not put patients at any additional risk.¹⁸ It is the manufacturer's responsibility to determine when a 510(k) submission to FDA is required.¹⁹

It is also the manufacturer's responsibility to validate the design of their new or modified devices to make sure they work properly, which includes the ability for that device to be safely reprocessed between uses.²⁰ Manufacturers must test their devices and collect evidence to show that reprocessing will consistently result in a device that meets certain decontamination specifications.²¹ Proper validation should test all stages of reprocessing, and "the characteristics

of the user population and operating environment [should be] considered.”²² Once a medical device is sold and in use in the United States, FDA monitors the device primarily by relying on manufacturers and hospitals to observe when a device is working and to report when it is not. Manufacturers are required to submit medical device reports (MDRs) within 30 days of learning information that reasonably suggests a device may have caused or contributed to a death or serious injury.²³ Within 10 work days, hospitals must report serious injuries potentially caused by devices to the manufacturers, and report deaths connected to a device to both the manufacturers and FDA.²⁴ Additionally, the Medical Product Safety Network (MedSun) provides a secure online mechanism for 250 participating hospitals to report adverse events related to medical devices before a patient is injured or dies.²⁵ Finally, anyone, including hospitals and patients, may submit a voluntary “MedWatch” report to alert FDA to any suspected device issues.

FDA receives over one million MDRs each year, and relies on a small number of human reviewers to spot safety issues.²⁶ MDRs are often incomplete and lack key details, in part because FDA encourages quick filing with additional follow-up as more information is learned, and thus expects

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initial submissions to be incomplete. MDR reports are primarily useful once FDA has already identified a problem; the agency can then search the MDR databases to identify similar or related reports. MDRs are extremely difficult to search and query, however. A simple spelling error or inconsistency in naming products can prevent the agency from tracking or identifying MDRs related to specific devices or patient outcomes.²⁷ Moreover, MDRs are not designed to identify trends, alert FDA to emerging problems, or track particular devices over time.

Finally, FDA can also require device manufacturers to conduct a postmarket surveillance study of the safety or effectiveness of a device (a section 522 postmarket surveillance study). FDA sets out specific questions, and the manufacturer designs and conducts a study to answer those questions over a three year period. The manufacturer then produces a Postmarket Surveillance Study Report setting forth the results of its study.²⁸ These section 522 postmarket surveillance studies have been criticized by some observers because there is very little infrastructure developed to assist device manufacturers as they design and carry out the studies, including a lack of device registries or identification codes that allow manufacturers to track and link devices to outcomes.²⁹ Additionally, there are few incentives for clinicians and patients to participate in the studies, which may make it difficult for manufacturers to obtain the information they need.³⁰ As an example, while FDA has sought studies on 104 metal-on-metal hip products. However, just 24 products have FDA-approved study plans while the remaining 80 are listed as having either a “Plan Pending” or a “Plan Overdue.”³¹

Currently, device manufacturers are essentially responsible for determining when a new clearance is required, how much information to report about adverse events, and how to conduct safety studies. This forces FDA to rely too heavily on manufacturers and user facilities to alert the agency to problems, help it accurately assess the severity of a potential safety issue, and move quickly to address it.

The Current Surveillance System to Ensure Medical Devices are Safe and Effective is Inadequate

The investigation found that FDA’s current regulatory system for monitoring the safety of devices

failed to quickly identify and resolve the spread of duodenoscope-linked, antibiotic-resistant infections. It took FDA almost a year and a half from the time the agency first became aware that closed-channel duodenoscopes could remain contaminated after proper cleaning to alert hospitals and the public. While responsibility for the slow response is shared among Olympus and the other device manufacturers, hospitals, and FDA, the investigation overall demonstrates that FDA's device surveillance system is overly-reliant on device manufacturers and user facilities to make quick and complete reporting of safety issues over their own competing priorities.

FDA relies on device manufacturers and hospitals to provide information so that FDA has the data it needs to assess the safety and effectiveness of medical devices. The regime relies on compliance with the law and self-reporting from device manufacturers and hospitals, ignoring the reality that manufacturers and health care providers have strong competing priorities that weigh against rapid and robust disclosure, such as moving new products to market quickly and avoiding costly litigation.

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The current postmarket surveillance system relies on device manufacturers to self-monitor and self-report by: 1) determining when it is necessary to submit design modifications to FDA for review; 2) adequately testing that the devices work consistently in real-world settings; and 3) reporting when adverse events occur. The device manufacturers in this investigation failed to fully comply with any of these three regulatory requirements, providing a vivid example of the flaws with the current system.

FDA's reliance on manufacturers and hospitals to quickly and accurately report safety concerns related to devices stands in contrast to FDA's ability to independently monitor the safety of drugs.

FDA increasingly has access to information about the postmarket safety and effectiveness of drugs through its "Sentinel" surveillance system.³² Because all drugs carry a National Device Code (NDC), which is also included on all pharmacy insurance claims and electronic health records, FDA has been able to leverage the wealth of information available through these sources to identify potential problems with a particular drug and proactively monitor drugs that are new to the market or are of particular interest. Sentinel allows FDA to query databases that contain real-time information, reducing the agency's reliance on the information reported by drug manufacturers and hospitals. Sentinel has the added advantage of allowing the agency to assess the frequency of adverse events relative to the overall use of a drug and relative to the rate of adverse events for similar drugs.

At this time, no similar system exists for devices. While the Food and Drug Administration Amendments Act of 2007 required devices to have a Unique Device Identifier (UDI) placed on medical device labels and packages comparable to the NDC number for drugs, and the Food and Drug Administration Safety and Innovation Act of 2012 required that Sentinel be expanded to devices, the UDI requirement does not go into effect for all devices until 2020.³³ Of more significant concern, UDIs are not currently included in insurance claims, which contain the critical information necessary to draw conclusions about device safety and patient outcomes. Without widespread adoption of UDI in electronic health records and claims, FDA will remain overly reliant on information reported by manufacturers and hospitals and unable to utilize a Sentinel-like system to ensure critical information about problematic devices is rapidly identified.

As detailed below, Olympus, Pentax, Fujifilm, and Custom Ultrasonics failed to report to FDA the information necessary to make the current postmarket surveillance system work properly.

Hospitals also generally failed to provide manufacturers with required information about antibiotic-resistant infections linked to their devices or to proactively alert federal authorities to their concerns. As a result, FDA was unable to accurately assess and quickly react to the risks posed by closed-channel duodenoscopes.

Device Manufacturers Failed to Meet Regulatory Requirements and Endangered Patients

By the end of 2012, at least one duodenoscope manufacturer, Olympus, was aware that the new closed-channel duodenoscope the company had marketed since 2010 had the potential to remain contaminated even after cleaning and reprocessing according to manufacturers' instructions. Properly cleaning reusable devices like duodenoscopes is challenging, and failures to clean the devices correctly have resulted in patient infections in the past. An elevator wire channel located at the end of the duodenoscope allows doctors to move tools inserted through the duodenoscope

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to perform procedures.³⁴ In early duodenoscope models, the elevator wire channel remained open and exposed to the same type of contamination as the rest of the scope.

In an effort to protect this part of the scope from contamination, in 2010 Olympus introduced a new closed-channel model that sealed off the elevator wire channel with an "O-ring" designed to prevent exposure to any contaminants from a patient.³⁵ The other two duodenoscope manufacturers, Pentax and Fujifilm, similarly moved to closed-channel duodenoscopes although Pentax did so considerably earlier.

After a lengthy investigation by FDA throughout 2014 and 2015, it is now evident that, unlike open-channel duodenoscopes, closed-channel duodenoscopes can trap and transmit bacteria even when the devices are cleaned according to manufacturers' instructions. Moreover, at least one manufacturer, Olympus, the manufacturer of 85 percent of the duodenoscopes used in the United States and in 19 of the 25 reported incidents, was aware of the problems well before FDA's findings, but failed to adequately alert either FDA or the hospitals and patients using these scopes.

Olympus knew in 2012 that the design of its closed-channel duodenoscope could prevent effective cleaning.

Erasmus Medical Center, Rotterdam, Spring 2012

In January 2012, there was an outbreak of antibiotic-resistant infections affecting 30 patients at Erasmus Medical Center in Rotterdam, the Netherlands. Hospital staff traced the infections to patients undergoing ERCP, and then directly to an Olympus TJF-Q180V closed-channel scope first marketed in the United States in mid-2010.³⁶

After Erasmus contacted Olympus, the hospital and manufacturer jointly asked Dr. Arjo Loeve of the Delft University of Technology to conduct an independent investigation into the Olympus duodenoscope.³⁷ Dr. Loeve's investigation took place on April 23, 2012, at Olympus Netherlands headquarters with assistance from an Olympus employee flown in for the

purpose of correctly disassembling the scope.³⁸ The investigation was observed by two Olympus Europa employees, three Olympus Netherlands employees, and six staff from Erasmus Medical Center.³⁹

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The study identified two critical design flaws in the TJF-Q180V duodenoscope that made it difficult to clean reliably. First, Dr. Loeve found a series of tiny crevices that are too small to clean with a brush but large enough to allow in and trap bodily fluids and bacteria. In his report, Dr. Loeve points in particular to the space created by the axial clearance of the elevator, the area behind the curve of the elevator, and the hinges of the elevator as “locations where lingering and/or increasing moisture and/or biological materials are quite likely.”⁴⁰

Picture from USA TODAY

Dr. Loeve also found that poor-quality sealing at the end of the scope is a potential mechanism for transmitting bacteria between patients. Dr. Loeve describes cracks in the material around the

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camera, scale that was found behind the glass that covers the camera face, and open air bubbles, which can trap contaminants.⁴¹ The O-ring, which seals off the elevator channel from contamination, was torn, worn, and contained “brownish scale,” which indicates the O-ring may not have created a tight seal.⁴² This is particularly dangerous because the closed elevator wire channel, unlike the open channel of the previous duodenoscope model, does not undergo HLD. Dr. Loeve concluded that it was “very likely [the] O-ring has not done its job” and “reliable sealing by means of the O-ring cannot be guaranteed.”⁴³

Ultimately, in his May 2012 report, Dr. Loeve concluded that there needed to be a series of design changes to the TJF-Q180V scope to ensure it could be effectively decontaminated between uses. Dr. Loeve suggested changing the design of the scope to either have multiple sealing barriers or return to an open channel, to regularly ensure proper sealing between the O-ring and the scope, to frequently replace the O-ring to ensure the sealing mechanism remains functional, to alter the design to make various cracks and spaces larger so that a cleaning brush can reach them, and to rework the cleaning instructions to better address the hard-to-clean spaces in the scope.⁴⁴

On May 25, 2012, one month after five Olympus officials participated in the examination of the relevant scope at Delft University and ten days after the Delft report finding that the design of the scope hinders reprocessing was published, Olympus filed an MDR with FDA regarding the infections at Erasmus. The MDR stated that “the device was being investigated by independent organization [sic]” and that “the photograph of the distal end of the device which was sent from OLYMPUS NEDERLAND showed the debris around the objective lens.”⁴⁵ While the MDR provided FDA with notice that the infections were linked to the scope, it was fundamentally misleading. The MDR did not discuss the findings of the Loeve report, misstated the number of patients impacted, and specifically stated it could not “conclusively determine the cause [sic] this event,” claiming that “it can be considered as a possible cause of this phenomenon that the patient infected from other than the endoscope and procedure such as environmental factor in the facility

[sic].”⁴⁶

Following Dr. Loeve’s report, the Dutch National Institute for Public Health and the Environment (RIVM) requested additional documents and information from Olympus and Erasmus and produced a follow-up report in July 2013 that confirmed many of Dr. Loeve’s findings.⁴⁷ The RIVM report agreed with Dr. Loeve that “the construction of the endoscope hinders optimum manual cleaning.”⁴⁸ The RIVM report similarly confirmed that Olympus had no substantive response to Loeve’s concern about the O-ring, although RIVM could not rule out that the scale seen by Loeve was a result of previous repairs made to the scope rather than O-ring failure.⁴⁹

“The construction of the endoscope hinders optimum manual cleaning.”
– RIVM

Olympus did not update FDA regarding the events at Erasmus Medical Center until March 2015, and the company still did not fully describe the findings of the Delft or RIVM reports.⁵⁰

University of Pittsburgh Medical Center Presbyterian Hospital, Pittsburgh, fall 2012

A few months after Dr. Loeve’s report first raised alarms about whether the Olympus closed-channel duodenoscope could be consistently disinfected by following the manufacturer’s cleaning

instructions, Olympus was contacted by officials at the University of Pittsburgh Medical Center Presbyterian hospital in Pittsburgh, Pennsylvania (“UPMC”).⁵¹ In the fall of 2012, UPMC experienced an outbreak of CRE, infecting about 13 patients who had undergone ERCP procedures with Olympus duodenoscopes.⁵² Repeated cultures of one particular duodenoscope by UPMC staff found bacteria in the biopsy and water channels even after the scope had been reprocessed three times.⁵³

After UPMC traced the infections back to the device, Olympus and an outside consulting group, ECRI Institute, evaluated UPMC’s reprocessing procedures. ECRI found that UPMC’s reprocessing was “consistent with standard practice and manufacturer recommendations.”⁵⁴ ECRI told UPMC officials that it could not make a “definitive” assessment about whether “there is a defect within the endoscope that would provide a reservoir for bacteria” because the small crevices in the scope made it impossible for ECRI to fully examine the device.⁵⁵

When Olympus officials raised the possibility that the hospital’s Custom Ultrasonics AERs could be at fault, UPMC officials went so far as to purchase an Olympus AER and demonstrated that the use of Olympus’ own reprocessing machine did not prevent scopes from remaining contaminated after cleaning.⁵⁶ On December 18, 2012, Olympus filed an MDR with FDA, which documented some of the events at UPMC and the findings of ECRI. This MDR appears to have never been entered into FDA’s system.⁵⁷

Additional independent testing, Jan 2013-2014

Documents obtained from Olympus show that from December 2012 through at least the summer of 2014 the company engaged independent laboratories to test company’s closed-channel duodenoscopes for contamination, to assess whether the devices could be consistently disinfected, and to validate revised cleaning procedures. On January 8, 2013, before the infections at Virginia Mason had occurred, the French medical device evaluation company Biotech-Germande completed a report evaluating the Olympus duodenoscope with the same serial number as the

scope involved in the December 2012 infections at Clinique de Bercy in France. The evaluation showed that “three cleaning/disinfection procedures were needed to eliminate the contamination that was initially present in the internal channels of the endoscope” and noted the “difficulty of eliminating all contamination present at the air/water and suction/biopsy valves and the operator channel cap through the application of a standard manual cleaning/disinfection procedure.”⁵⁸ A follow-up study in July 2014 further confirmed “that after a complete reprocessing procedure consistent with the guidelines of the Ministry of Health and the recommendations of [Olympus] a contamination may persist at the distal end of the endoscope”⁵⁹ Studies at Bonn University conducted from March to November 2013, did confirm that a separate closed-channel duodenoscope was successfully cleaned using an Olympus AER.⁶⁰

European Alerts

By the end of 2012, Olympus had two clear examples of contaminated scopes spreading antibiotic-resistant infections even after correct reprocessing but neglected to alert hospitals or regulators in the United States. While Olympus left American doctors and hospitals in the dark about the duodenoscope design issues, in January 2013, Olympus sent a letter informing some European hospitals that they needed to carefully follow all reprocessing instructions and to “pay particular attention to the detailed pre-cleaning instructions, especially for the distal end and forceps elevator.”⁶¹ By the time Olympus sent the letter, the company was aware of at least three

duodenoscope-linked outbreaks impacting about 46 patients in three different countries; however, the letter only references “*a recently reported case*” of a contaminated TJF-Q180V scope.⁶²

Again, in August 2014, Olympus disseminated in Europe an urgent field safety corrective action. The August 2014 safety communication references “*a few complaints of residual debris in the distal end of the TJF-Q180V duodenoscope after reprocessing.*”⁶³ By that time, Olympus knew of at least ten different instances of hospitals reporting contaminated TJF-Q180V scopes spreading antibiotic-resistant infections between patients.⁶⁴

FDA Investigation

In September 2013, after CDC alerted FDA to an outbreak of infections at Advocate Lutheran General Hospital linked to a Pentax duodenoscope, and CDC confirmed that Advocate Lutheran reprocessed scopes correctly according to the manufacturer’s instructions, FDA began an investigation into closed-channel duodenoscopes. Throughout 2014, FDA worked to better understand the extent of the problem and to develop recommendations. It appears that at the time the investigation was initiated, FDA was unable to locate either the Erasmus or UPMC MDRs filed by Olympus and was without the benefit of reports from Dr. Loeve’s Delft University or RIVM. By April 2014, FDA had independently sought validation data from the duodenoscope manufacturers in order to determine if the cleaning instructions worked reliably. FDA became aware of and obtained a copy of the Delft report only sometime after September 2014; had Olympus shared the existence of the report earlier, it likely would have sped FDA’s investigation and led to more rapid alerts from both Olympus and the agency.

Instead, Olympus did not acknowledge the problem in the United States until February 19, 2015, six months after the urgent safety communication in Europe and almost three years after the Delft report. In May 2015, Olympus provided additional updates to their reprocessing instructions and distributed a new brush to help ensure that duodenoscopes are clean before undergoing HLD – a

brush that was available in Europe for nearly five years before it was provided in the United States. Had hospitals been alerted to the risk and the need to use increased efforts to ensure that duodenoscopes were appropriately disinfected, some if not all of the infections, including in Seattle, may have been prevented.

Olympus's failure to take action and alert regulators likely contributed to the at least 141 patient infections linked to Olympus duodenoscopes that occurred in domestic hospitals between the spring of 2012, when Olympus was well aware of potential flaws with the device, and February of 2015, when the company finally alerted doctors and hospitals in the United States.

Olympus failed to meet its regulatory obligations.

Olympus's failure to act upon the information it knew about the problems decontaminating closed-channel duodenoscopes and the spread of deadly infections is consistent with the company's failure to meet its obligations at each step of the device regulatory process. During its investigation in 2014 and 2015, FDA determined that Olympus failed to seek required clearance for the modification from an open to closed-channel device, failed to validate the closed-channel duodenoscope cleaning instructions to make sure they worked consistently, and failed to fully report information it knew about the adverse events linked to its device.

Olympus did not clear its duodenoscope design modification with FDA.

Manufacturers of Class II devices like duodenoscopes are required to make a 510(k) submission in order to market a new device, an existing device for a new purpose, or a device that is changed or modified in a way that might implicate its safety or effectiveness.⁶⁵ This allows FDA to ensure that the modified device remains "substantially equivalent," or at least as safe and effective, as a device that is already legally on the market.⁶⁶ It is the manufacturer's responsibility to determine if and when a 510(k) application should be submitted to FDA.⁶⁷

Olympus did not file a 510(k) application for the TJF-Q180V duodenoscope because it determined the new model was similar to a previous device, the TJF-Q160, approved in 2008. However, unlike the TJF-Q180V, the TJF-Q160 has an open elevator wire channel. FDA subsequently determined Olympus was wrong to assert that the TJF-Q160 and TJF-Q180V are substantially equivalent devices, and found that the change from an open to a closed elevator channel "impacts the safe use of the device" because the newly sealed elevator channel "prevent[s] sterilization and high level disinfection."⁶⁸ FDA notified Olympus that it should have made a 510(k) submission to account for the substantial changes between the TJF-Q160 and the TJF-Q180V and, in March 2014, required the company to belatedly make that submission. FDA is currently in the process of evaluating those documents to assess the substantial equivalency of the elevator channel sealing mechanism.

Olympus failed to ensure duodenoscope cleaning instructions worked before selling closed-channel duodenoscopes to hospitals.

The investigation also found that Olympus has been selling its closed-channel duodenoscope since 2010 without sufficiently testing its cleaning instructions to ensure that they actually work in real-world settings, and that Olympus knew that its testing data was insufficient since at least 2013.

FDA requires device manufacturers to validate the design of their devices, which includes the ability for that device to be safely reprocessed between uses.⁶⁹ In other words, manufacturers must

test their devices and collect evidence to show that reprocessing will consistently result in a device that meets certain decontamination specifications.⁷⁰ Proper validation should test all stages of reprocessing and should consider “the characteristics of the user population and operating environment.”⁷¹

However, in July 2013, following the infections at Erasmus Medical Center in Rotterdam, RIVM examined Olympus’ validation of the TJF-Q180V reprocessing instructions and found the data analysis “unacceptable as a demonstration of effective cleaning.”⁷² RIVM concluded that the data

Olympus provided to show that manual cleaning could decontaminate the elevator mechanism “left so much to be desired that it is not possible

to support the conclusion drawn by the manufacturer, namely that the cleaning and disinfection procedure for the elevator is effective.”⁷³ Olympus also did not provide

RIVM with information to substantiate that the

O-ring effectively seals the elevator wire

channel from contamination or attempt to show

that the leak testing that hospitals are supposed to conduct during reprocessing is an accurate way

of assessing when an O-ring is wearing out and in need of maintenance from the manufacturer.⁷⁴

After requesting Olympus’s validation data in April 2014, FDA reached the same conclusion –

[Olympus’s reprocessing data] is “unacceptable” and left so much to be desired that it is not possible to support the conclusion . . . that the disinfection procedure. . . is effective.”
– RIVM

Olympus did not have sufficient data to show closed-channel duodenoscopes could be reliably cleaned with an adequate margin of safety.

In the 19 months between RIVM’s conclusion that Olympus did not have sufficient validation data and Olympus’ first safety notice, at least 49 patients in the United States were infected with antibiotic-resistant bacteria connected to an Olympus closed-channel duodenoscope.

At the time Olympus’ closed-channel duodenoscopes were first sold in the United States, FDA relied on manufacturers to attest that their devices had been validated effectively before being marketed. Unsurprisingly in view of the RIVM findings, in April 2014 when FDA similarly asked Olympus to produce suitable data to show their cleaning instructions actually worked, the company could not do so.⁷⁵ The faith that patients, doctors, hospitals, and public health officials placed in Olympus to thoroughly test their cleaning instructions before putting devices in the marketplace was clearly misplaced.

In February 2015, Senator Murray requested FDA update its draft reprocessing guidance for reusable devices, and on March 17, the agency issued final guidance, “*Processing/Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling*.”⁷⁶ This final guidance requires manufacturers of high-risk reusable devices such as duodenoscopes to provide FDA with their actual reprocessing data when applying for clearance to market devices so that FDA can assess the validity of cleaning instructions for itself. While the guidance is a useful step, under current law, manufacturers of reusable devices are still not required, as a condition of market clearance, to produce data that actually demonstrates the devices can be reliably and repeatedly cleaned in real world conditions.

Olympus submitted incomplete and misleading medical device reports to FDA.

Finally, while Olympus generally submitted MDRs to account for duodenoscope-linked infections the company was aware of, Olympus did so in such a cursory manner as to make it nearly impossible for the agency to accurately assess the scope and severity of the infections linked to duodenoscopes. Because device manufacturers and importers are the only entities required to submit adverse event reports to FDA when a device is linked to a serious injury, the agency relies heavily on the accuracy of manufacturers' reports to track problems with medical devices.⁷⁷

Some Olympus MDRs, particularly those submitted for outbreaks in Europe, understate the number of patients affected,⁷⁸ point to environmental contamination as a source of the infections rather than problems with the device itself,⁷⁹ and fail to provide the full information available to Olympus. Following the reports of contaminated scopes at Erasmus Medical Center and Clinique de Bercy in France, Olympus received results from independent labs that found the duodenoscopes linked to infections in those hospitals could contain bacteria even after being cleaned correctly, but never updated their adverse event reports or communicated that information to FDA.

As a result of inspections conducted in 2015, FDA found that Olympus "fail[ed] to adequately develop, maintain, and implement written MDR procedures" as mandated by adverse event reporting regulations and did not have a consistent process for "submit[ting] all information reasonably known to it for each event."⁸⁰ While FDA's findings regarding the MDRs submitted by Olympus are certainly correct, the violations also understate the real impact of Olympus' larger failure to alert regulators in the United States and Europe about significant problems in cleaning the TJF-Q180V closed-channel scope.

Pentax and Fujifilm also failed to comply with regulatory requirements.

While the majority of the infections that occurred between 2012 and spring of 2015 were connected to an Olympus duodenoscope, closed-channel devices manufactured by Pentax and Fujifilm were also linked to six outbreaks and at least 53 antibiotic-resistant infections during this time. Pentax sells about 12 percent of the duodenoscopes used in the United States and Fujifilm about three percent.⁸¹ These duodenoscope manufacturers contributed to the dangerous superbug and other antibiotic-resistant infections linked to ERCP procedures at hospitals in the United States and around the world by failing both to comply with the same basic regulatory expectations as Olympus and communicate thoroughly with FDA about the outbreaks.

Fujifilm failed to clear their duodenoscope design modifications with FDA.

Similar to Olympus, FDA determined that Fujifilm never made a 510(k) submission for the modifications in the design of its closed-channel scope ED-530XT. ⁸² Fujifilm had concluded that there were only minor changes between ED-530XT and the already-approved open-channel model ED-450XT5. However, FDA's inspection identified least four potentially substantial differences between the ED-450XT5 and the ED-530XT. In August of 2015, FDA sent a 510(k) status letter to Fujifilm summarizing these findings and requested a 510(k) application for the ED-530XT.⁸³ FDA has not yet determined whether Pentax should have submitted a 510(k) application to account for the changes between the Pentax ED-3490TK and ED-3670TK.⁸⁴

Pentax and Fujifilm failed to properly validate their duodenoscope reprocessing instructions.

Once FDA launched its investigation into closed-channel duodenoscopes, it requested the data from Pentax and Fujifilm demonstrating that each company's closed-channel duodenoscope could

be consistently cleaned. Also like Olympus, both Pentax and Fujifilm were unable to produce the required underlying data to show that the cleaning instructions were consistently effective. In fact, after FDA inspections of Fujifilm plants in April and May 2015, the agency observed multiple flaws in Fujifilm's validation process including that the company did not evaluate the O-ring,⁸⁵ performed validation on a mock-up of a duodenoscope channel rather than the actual device,⁸⁶ did not produce the appropriate reduction in bacterial spores during ethylene oxide sterilization validation,⁸⁷ and did not evaluate the design of the closed-channel model under actual or simulated conditions of use.⁸⁸

FDA inspections also found that Pentax had validated its HLD and sterilization protocols for the ED-3670TK duodenoscope using an entirely different model of scope and could not show that the two duodenoscopes responded comparably to reprocessing.⁸⁹ Moreover, Pentax tested sterilization of the scope with a different mixture of gas than it instructed hospitals to use.⁹⁰

On December 23, 2015, FDA announced that new Fujifilm reprocessing instructions that included additional brushing, washing, and flushing were sufficiently validated, and "demonstrate consistent and reliable cleaning and high level disinfection."⁹¹ Meanwhile, Pentax has not yet demonstrated to FDA that its new cleaning instructions were validated, leaving doctors and hospitals in the disconcerting position of using a device without cleaning instructions they can feel confident about.

Pentax and Fujifilm submitted late and incomplete medical device reports.

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Similarly, Fujifilm and Pentax failed to meet their obligations to self-report serious illnesses and deaths that may have been caused by their duodenoscopes. After inspecting manufacturers' files in 2015, FDA found that both companies had substandard MDR reporting practices. Pentax failed to "adequately develop, maintain, and implement written MDR procedures" or "internal systems that provide for timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements."⁹² Meanwhile, Fujifilm lacked procedures for "receiving, reviewing, and evaluating complaints."⁹³

These failures may well explain why neither Fujifilm nor Pentax appears to have filed a single adverse event report related to antibiotic-resistant infections and closed-channel duodenoscopes with FDA for any incidents in any foreign country until the fall of 2015 despite the regulatory requirement to report adverse events that occur anywhere in the world for any device sold in the United States.⁹⁴ The Americas are only about 36 percent of Pentax's business worldwide with 15 percent in the Asia Pacific region, 49 percent in Europe, the Middle East, and Africa, and less than one percent in Japan.⁹⁵ Fifty percent of Fujifilm duodenoscopes are sold in Europe, 22 percent in Asia, and 18 percent in Latin and South America.⁹⁶ Since Pentax and Fujifilm scopes were collectively linked to six outbreaks domestically by Spring 2015, it is hard to imagine that no infections during this time were connected to the more than 90 percent of Fujifilm scopes in use outside of North America and more than 64 percent of Pentax duodenoscopes used outside of North and South America.

Overall, FDA inspections documented that all three duodenoscope manufacturers put patients' lives in jeopardy by failing to meet their obligations at each step of the regulatory process. The manufacturers failed to seek FDA clearance for their modified devices when they changed to the

closed-channel design. When confronted with evidence that the design of closed-channel duodenoscopes was contributing to the spread of infections across the United States and worldwide, the duodenoscope manufacturers did not take adequate action to alert device users or regulators, allowing its device to spread superbug and other serious infections among ERCP patients for years.

Custom Ultrasonics' automated endoscope reprocessors likely contributed to patient infections.

On November 13, 2015, FDA took the unusual step of issuing a mandatory recall of all of the approximately 2,800 Custom Ultrasonics AERs in hospitals and clinics across the United States. FDA is so concerned about Custom Ultrasonics AERs' ability to perform as marketed that the agency deemed a mandatory recall necessary to protect the public's health, and has recommended that hospitals using Custom Ultrasonics AERs switch to alternative methods of HLD.⁹⁷

HELP Committee staff has been able to confirm that Custom Ultrasonics machines were used by at least nine out of 16 domestic hospitals that experienced infections after ERCP procedures accounting for about 141 patient infections at:

- UPMC Presbyterian Hospital, Pittsburgh, PA
- NYP/Weill Cornell Medical Center, New York City, NY
- UMass Memorial Hospital, Worcester, MA
- Advocate Lutheran General Hospital, Park Ridge, IL
- Hartford Hospital, Hartford, CT
- Massachusetts General Hospital, Boston, MA
- UCLA Medical Center, Los Angeles, CA
- Carolinas Medical Center, Charlotte, NC
- Thomas Jefferson University Hospital, Philadelphia, PA

Picture from www.customultrasonics.com

Considering that only about ten to 20 percent of the AERs used in American hospitals are Custom Ultrasonics AERs, it appears the defective machines played a significant role in allowing the duodenoscopes to remain contaminated between uses.

However, it is also clear that duodenoscope-linked infections cannot be solely attributed to Custom Ultrasonics machines. Erasmus Medical Center, Virginia Mason Hospital, Froedtert Hospital, and Advocate Good Samaritan Hospital all experienced contaminated duodenoscopes while using other brands of AER machines. Additionally, UPMC, which used Custom Ultrasonics machines, took the unusual step of purchasing an Olympus-made AER and demonstrated that their Olympus

closed-channel duodenoscope remained contaminated even after cleaning it in Olympus' own AER.

Similar to washing machines, AERs flush liquid chemicals through scopes to destroy lingering contaminants after the device is hand cleaned with small brushes in order to achieve HLD. If an AER is not working correctly, it may not completely disinfect the scopes. Custom Ultrasonics' AERs do not appear to have consistently provided HLD when used to clean duodenoscopes after procedures, and the company, like the duodenoscope manufacturers, appears to have repeatedly abused the expectations of the current regulatory system.

FDA first cleared the Custom Ultrasonics AER for use in 1984 but the company has faced regulatory challenges dating back to at least 2005.⁹⁸ After FDA inspections in 2005-2007 revealed that Custom Ultrasonics failed to comply with regulations designed to ensure that devices are manufactured according to certain standards of quality, Custom Ultrasonics and FDA entered into a consent decree in 2007 preventing Custom Ultrasonics from manufacturing and distributing any devices – including AERs.⁹⁹ Although the company was able to resolve some of the issues and resume manufacturing five months later, FDA subsequently found Custom Ultrasonics in violation of the terms of the consent decree at least three separate times since 2008, including failure to seek 510(k) clearances for significant changes to its devices.¹⁰⁰

In the spring of 2015, FDA asked for data from all AER manufacturers. In April 2015, an inspection of the Custom Ultrasonics plant in Ivyland, Pennsylvania found Custom Ultrasonics:

- *Never validated the compatibility of its AERs with closed-channel models of duodenoscopes;*

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- Did not validate their AERs with specific types of HLD cleaning solutions;
- Did not validate the effectiveness of pre-filters that prevent large particulates and debris from contaminating devices; and
- Did not sufficiently validate the water filtration system.¹⁰¹

Ultimately, FDA concluded that Custom Ultrasonics machines could not consistently provide the adequate margin of safety required by liquid chemical sterilant and HLD-specific guidance.¹⁰²

Overall, the investigation found that the current regulatory regime places obligations on device manufacturers that each of the four manufacturers above repeatedly failed to meet. At each step of the regulatory process – the determination of whether new device clearances need to be sought, quality testing that truly proves a device will consistently perform in real world settings, and prompt and complete reporting of all required adverse events – each of the four device manufacturers discussed above failed to meet these obligations. These failures are directly responsible for the spread of antibiotic-resistant infections in already critically ill patients.

Hospitals Were Slow to Report Infections

While this investigation has demonstrated that duodenoscope manufacturers and Custom Ultrasonics failed to quickly and comprehensively report problems with their devices to FDA, the investigation has also revealed a similar problem among hospitals. At least 16 domestic hospitals,

primarily large, sophisticated health systems, identified outbreaks of antibiotic-resistant infections linked to ERCP, but none actually followed all of the required steps to promptly notify manufacturers or, in cases of death, FDA.

FDA regulations require hospitals to submit an adverse event report to a device manufacturer within ten working days of becoming aware of information that reasonably suggests that a device “may have caused or contributed” to a serious injury or death.¹⁰³ The hospital is supposed to report the information to the manufacturer on FDA form 3500A or an approved electronic substitute, which includes a variety of information about the facility, the patient, and what happened, in order to help the manufacturer meet their own reporting obligations to FDA.¹⁰⁴

Because they are on the front lines of treating patients, doctors and hospitals are often the first to recognize device related problems. Health care providers thus play a critical role in alerting manufacturers and federal regulators to suspected issues. However, conversations between Senator Murray’s HELP Committee staff and hospital staff, state and local health departments, and manufacturers have revealed a disconcerting lack of awareness that these reporting obligations even exist.

Hospitals did not comply with mandatory requirements to report information to manufacturers.

As part of this investigation, HELP Committee staff spoke with staff at eight hospitals that had infections linked to closed-channel duodenoscopes before or around September 2013 – when FDA first understood that some duodenoscopes remained contaminated after cleaning according to manufacturers’ instructions.¹⁰⁵

These conversations demonstrated that numerous hospitals were able to identify, track, and contain superbug and other antibiotic-resistant infections within their hospitals, but not a single hospital that experienced infection outbreaks tied to the duodenoscopes appears to have sent the required adverse event form to the device manufacturers. Several hospitals appear to have failed entirely to alert the device manufacturer in any way.

It appears that not a single hospital that experienced infection outbreaks linked to the duodenoscopes sent the required adverse event form to the device manufacturers.

Multiple hospitals across the country engaged in exemplary public health work to identify clusters of antibiotic-resistant infections, isolate the source, and contain the problem. At least 16 hospitals across the United States were able to identify that they had patients with unusual infections and trace those infections back to ERCP procedures performed with duodenoscopes. These investigations were often complicated and sophisticated. For example, Virginia Mason, with the assistance of the Washington State Department of Health, undertook enhanced surveillance efforts

that identified a cluster of patients infected after ERCP. From that cluster, hospital officials were able to identify a unique isolate that was then used to trace the infections.

Similarly, UMass Hospital in Worcester, Massachusetts used isolate testing and DNA fingerprinting to confirm that liver transplant patients were infected with the same strain of antibiotic-resistant bacteria. Massachusetts General Hospital in Boston and NYP/Weill Cornell Medical Center in New York City conducted in-depth retrospective analyses that retroactively linked patient infections with ERCP procedures. It is likely that many hospitals with fewer resources similarly experienced infections but did not identify or track the infections.

Most hospitals also alerted either their state or local health departments about the infections. States have varying reporting requirements and not all hospitals are required to report infections to health department officials, or may be required only to report certain types of infections or infections impacting a large number of patients.¹⁰⁶ Even in cases when reporting was not required, however, hospitals generally appear to have communicated with their local or state officials about outbreaks. However, with the exception of Advocate Lutheran General Hospital, and Virginia Mason hospital which worked with a CDC staffer embedded in the King County Health Department who kept the agency informed, no hospital directly notified CDC, and there is no federal reporting requirement for hospitals to do so.

Startlingly, after identifying the source of the outbreaks, none of the eight hospitals entirely fulfilled their legal obligation to quickly alert manufacturers or FDA to adverse events at their hospitals traced to devices. Certain hospitals, including UMass, Carolinas Medical Center and Thomas Jefferson, failed entirely to alert manufacturers to problems, leaving Olympus, Fujifilm, Pentax, and FDA unaware of the outbreaks of infections potentially caused by contaminated duodenoscopes. Some hospital staff have explained they did not inform manufacturers, even after tracing infections back to ERCP procedures, because they could not demonstrate that a particular

scope harbored contamination, or be entirely certain that a problem with a specific duodenoscope caused a particular illness or cluster of infections among ERCP patients.

When hospitals did report adverse events, it was generally late, notification was made informally by phone or email, and reports did not include all of the information necessary for the manufacturers to submit accurate and complete information to FDA. Olympus relayed that none of the 12 domestic hospitals with outbreaks linked to Olympus scopes sent the required FDA form 3500A to the manufacturer.

Moreover, UPMC, NYP Weill/Cornell Medical Center, Advocate Lutheran, and Virginia Mason notified manufacturers of a potential problem months after they were aware of the connection. For example, by December 2013, Virginia Mason knew that duodenoscopes were contaminated and spreading antibiotic-resistant infections between patients but did not alert the manufacturer to the issue until July 2014.¹⁰⁷ When a team from Olympus evaluated Virginia Mason's reprocessing procedures in the fall of 2013, the hospital never mentioned the infections.¹⁰⁸ Hartford Hospital reported a patient tested positive for "bacterial micro-organisms" after an "unspecified procedure," vague information at best. Olympus followed up but received no response from the hospital.¹⁰⁹ Pentax MDRs also documented difficulty obtaining information from Massachusetts General Hospital, receiving no response after multiple requests for information.¹¹⁰

Overall, not one of the hospitals that had identified infection outbreaks by the time FDA became aware of the problem in September 2013 notified the manufacturer within the period dictated by

Hospital	Notified the Manufacturer *	Notified FDA *	Notified CDC	Notified Patients	Notified State/Local Health Departments **
UPMC Presbyterian Hospital, Pittsburgh, PA	Late	Late	No	Unk	Yes
NYP Weill/ Cornell Medical Center NYC, NY	Late	Late	No	Unk	Yes
UMass Memorial Hospital, Worcester MA	No	No	No	Yes	Yes
Advocate Lutheran General Hospital, Park Ridge IL	Late	Yes	Yes	Yes	Yes
Froedtert Hospital, Milwaukee WI	Late	Unk	No	Unk	Unk
Virginia Mason Hospital and Medical Center, Seattle WA	Late	Late	Indirectly	Late	Late
Thomas Jefferson University Hospital, Philadelphia, PA	No	No	No	No	Yes

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* Required

** May be required depending on the state

Hospitals also generally failed to communicate directly with FDA and CDC. Hospitals are required to report information related deaths (but not serious injury) to FDA no more than ten days after becoming aware of the incident, and may always submit adverse event reports relaying other suspected problems to the agency.¹¹¹ While several hospitals did eventually submit MedWatch reports to FDA, less than one percent of all the adverse event reports were submitted by hospitals, suggesting that hospitals are not meeting their obligations to report deaths that devices may have caused or contributed to.¹¹² Moreover, hospital staff interviewed by Committee staff almost universally were unfamiliar with any obligation to report to FDA.

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months after linking infections to duodenoscopes, UPMC reported that the “source of the [infection] remains undetermined at this time.”¹¹³ The report included neither that UPMC’s reprocessing procedures had been validated by Olympus nor that the hospital was unable to decontaminate the duodenoscope after multiple attempts at reprocessing. NYP Weill/Cornell filed a MedWatch report on October 9, 2013 clearly explaining that the duodenoscopes could not be reliably cleaned, but filed the report seven months after identifying the duodenoscope elevator as a source of the infections.¹¹⁴ Virginia Mason also filed a MedWatch report but did so in May 2014, at least five months after connecting patient infections to duodenoscopes.¹¹⁵ No hospital that identified clusters of antibiotic-resistant infections linked to closed-channel duodenoscopes reported those infections to CDC until May 2013.¹¹⁶

Overall, hospitals’ slow approach left FDA with an inaccurate picture of the frequency and severity of these events. Reporting by the hospitals as a whole suggests that rather than collaborate to quickly alert regulators to a potential device problem, hospitals were reluctant to share unconfirmed information. Hospitals as a whole appear to have believed they had an obligation to report only what they could demonstrate beyond any doubt. Such narrow reasoning reveals a misunderstanding about hospital reporting requirements, which are triggered by information that *reasonably suggests* a device *may* have caused or contributed to a death or serious injury.¹¹⁷ Hospitals’ slow reporting may have had the effect of impairing FDA’s initial understanding of the number and severity of infections tied to duodenoscopes, and is further evidence of the need to move beyond self-reporting to identify and address issues posed by medical devices.

FDA Failed to Recognize the Prevalence of Duodenoscope-Linked Infections and Respond Quickly

FDA first became aware that closed-channel duodenoscopes could not be reprocessed consistently to prevent transmission of deadly superbug and other antibiotic-resistant bacteria between patients in September 2013, after CDC alerted them to infections at Advocate Lutheran General Hospital. By this point, at least 11 hospitals, including Virginia Mason, had experienced outbreaks linked to reprocessed duodenoscopes. Because of FDA’s reliance on a passive postmarket surveillance system, the agency had no way to identify this trend until the issue was directly brought to their attention.

FDA reviews reports filed by manufacturers and others largely by having staff with clinical backgrounds read the more than one million adverse event reports submitted every year.¹¹⁸ As discussed above, FDA does not flag incomplete reports because the agency expects MDRs to be filed before all the relevant information is known, and expects manufacturers to supplement the reports as they learn more. Therefore, it is challenging for reviewers to identify trends that might involve a relatively low number of incidents. Additionally, because there is no way to measure how a series of adverse event reports relate to the total number of devices and procedures, the system provides no way to assess the prevalence of adverse events.

In the spring of 2013 Advocate Lutheran General Hospital contacted CDC about an ongoing CRE outbreak, the only hospital to proactively contact the agency.¹¹⁹ CDC officials sent to the hospital in August 2013 were able to trace the infection back to the closed-channel Pentax duodenoscopes used in ERCPs *and* confirm that the scopes had been carefully reprocessed by the hospital.¹²⁰ CDC in turn alerted FDA that duodenoscopes were potentially transmitting bacteria even after being cleaned in accordance with the manufacturer's instructions.

At that point, FDA began an investigation into infections transmitted by closed-channel duodenoscopes. One of FDA's initial steps was to query their adverse event reporting system to determine if similar events had been reported elsewhere. When FDA initially queried its adverse event database after learning from CDC of the infections at Advocate Lutheran, FDA had received the following information about six outbreaks involving closed-channel duodenoscopes:

- 1) ***Erasmus Medical Center, Rotterdam, Netherlands.*** Notified in May 2012 that 16 patients had tested positive for *Pseudomonas aeruginosa* after undergoing an ERCP with an Olympus duodenoscope, and that an independent investigation was being conducted.¹²¹
- 2) ***UPMC Presbyterian Hospital, Pittsburgh, PA.*** Notified in November 2012 that ten to 13 patients may have been infected with CRE after undergoing a procedure with an Olympus duodenoscope.¹²² Also notified that CRE had been found on one of the scopes, and that the scopes tested positive for *Klebsiella pneumonia* on two separate occasions after multiple cultures. In October 2013, an additional report relayed that another scope tested positive for contamination.¹²³
- 3) ***Clinique de Bercy, Charenton-le-Pont, France.*** Notified in December 2012 that three patients were infected with *Escherichia coli* after undergoing an ERCP performed with an Olympus duodenoscope. Mentions that the scope is being sent to an independent lab for testing.¹²⁴

- 4) ***Charite-Universitätsmedizin, Berlin, Germany.*** Notified in April and July 2013, that five patients at Charite-Universitätsmedizin in Berlin were infected with *Klebsiella* after undergoing treatment with an Olympus duodenoscope that had been used earlier on a patient with the same infection. Two of the five infected patients died.¹²⁵
- 5) ***NYP/Weill Cornell Medical Center, NYC, NY.*** Notified in June 2013 that 15 patients at NYP/Weill Cornell Medical Center were infected with CRE after undergoing a procedure with an Olympus duodenoscope and that four different duodenoscopes tested positive for CRE even after the scopes had undergone HLD. Olympus also reported the hospital was not using the correct reprocessing procedures.¹²⁶
- 6) ***Advocate Lutheran General Hospital, Park Ridge, IL.*** Notified in July 2013 that a patient had undergone ERCP with a Pentax closed-channel duodenoscope and then developed a CRE infection. The hospital confirmed that its staff used proper reprocessing procedures, and that an organism had been found under the elevator on the duodenoscope.¹²⁷

Taken together these reports should have provided FDA with considerable information to suggest cleaned scopes were continuing to spread infection; however, the agency appears to have lost the report filed describing the 2012 outbreak at UPMC (it is not available in the agency database).

This left FDA without the key information that reported the earliest domestic antibiotic-resistant infections linked to a correctly reprocessed duodenoscope. It also appears that FDA's initial search of their adverse event report database did not identify the foreign adverse event reports that accounted for half of the incidents reported before September 2013. Accordingly, FDA's initial query may have left the agency with information about just one additional instance of closed-channel duodenoscope linked infections.

By the time FDA started its investigation, outbreaks of antibiotic-resistant infections had likely already occurred at Thomas Jefferson University, Virginia Mason, Carolinas Medical Center, and Froedtert hospitals. However, those outbreaks had not yet been reported to the agency, or, in some cases, to the device manufacturers. FDA appears to have been left with such incomplete information that it was unable to develop an accurate sense of the frequency and severity of these outbreaks. This lack of complete information made it difficult for the agency and outside experts to conclusively determine that mistakes in the cleaning and reprocessing of the duodenoscopes were not the source of the infections.

Throughout late 2013 and 2014, as the agency became aware of the clusters of infections in Pennsylvania, Massachusetts, Connecticut, Washington, Illinois, and Wisconsin, and the number of patients infected with potentially deadly bacteria continued to rise, FDA continued to investigate and collaborate with CDC and outside experts. FDA had not yet determined whether the infections occurred because hospitals did not correctly follow manufacturers' cleaning instructions or whether the closed-channel duodenoscopes could remain contaminated even after reprocessing was correctly carried out. FDA had also not yet developed supplemental reprocessing recommendations to ensure hospitals initiated enhanced cleaning procedures. As a result, FDA still had not issued any safety communication to alert hospitals to the risk posed by these devices.

In April 2014, FDA sought the validation data from duodenoscope manufacturers to show that they had properly tested their cleaning instructions to make sure that the data showed the instructions worked consistently. It was not until September 2014, when an FDA official met someone involved with the investigation of the outbreak in the Netherlands at a conference, that

FDA learned of the RIVM report detailing Olympus' lack of cleaning validation data almost a full year earlier. As a result, it took an additional year for FDA to receive the data, determine it was insufficient, and for the manufacturer to develop enhanced cleaning procedures cleared by FDA in the spring of 2015.

By late 2014, FDA had sufficient information to begin preparing a safety communication for hospitals. In January 2015, news reports revealed the infections in Seattle as well as more recent infections at UCLA and Cedar Sinai hospitals in California. On February 4, 2015, Senator Murray wrote to FDA seeking additional information about the infections, urging the agency to provide hospitals with safety information and to finalize the guidance for the cleaning of reusable devices that had been issued as a draft in 2010.¹²⁸

Following those events, U.S. federal agencies took the following steps in 2015:

- **February 19: FDA issues a Safety Communication.** FDA warns for the first time that duodenoscopes may transmit antibiotic-resistant infections between patients “even when manufacturer reprocessing instructions are followed correctly.”¹²⁹
- **March: The Department of Justice (DOJ) launches a criminal investigation into**

duodenoscope manufacturers. DOJ has since issued subpoenas to Olympus, Fujifilm, and Pentax as well as several hospitals for information related to duodenoscopes and antibiotic-resistant infections.

- **March 12: CDC issues an interim duodenoscope surveillance protocol.** CDC issued an interim protocol that instructs hospitals about how to culture and quarantine devices to assess whether their reprocessing procedures and manufacturers cleaning instructions are working correctly, and to identify contaminated scopes before they are used during procedures.¹³⁰
- **March 17: FDA finalizes reprocessing guidance for reusable devices.** The finalized guidance makes clear that FDA expects to see in 510(k) applications underlying data demonstrating that cleaning instructions actually work for certain reusable devices, including duodenoscopes.¹³¹
- **March–May: FDA inspects Olympus, Fujifilm, and Pentax manufacturing plants.** The inspections noted failures to make requisite 510(k) submissions by Olympus and Fujifilm, failures to maintain adequate MDR reporting systems, and failures to properly validate cleaning instructions.
- **April: FDA inspects Custom Ultrasonics’ facility.** Inspectors documented a series of violations including that the company had insufficient data to show their AERs worked effectively.
- **May 15 and 16: FDA convenes a meeting of the Gastroenterology-Urology Device Advisory Committee.** FDA issues an Executive Summary of the meeting indicating the agency is aware of at least nine outbreaks of infections linked to closed-channel duodenoscopes. The Advisory Committee discusses potential options for hospitals to ensure that devices are consistently cleaned after every procedure, including the culture and quarantine protocol developed and implemented by Virginia Mason staff.¹³² None of the three device manufacturers attended the advisory committee meetings.

- **August 4: FDA issues a safety communication for supplemental reprocessing.** The safety communication included four potential supplemental reprocessing measures including the microbiological culturing method put in place by Virginia Mason, Ethylene Oxide Sterilization, a liquid chemical sterilant processing system, or repeat HLD. None of these options are ideal. For example, ethylene oxide sterilization may pose health risks to hospital staff and microbiological culturing requires a hospital to purchase additional duodenoscopes.¹³³
- **August 12: FDA issues warning letters to Fujifilm, Pentax, and Olympus.** The letters included requests for the manufacturers to submit 510(k) applications so that FDA can evaluate the safety of the modification from an open to closed elevator wire channel.¹³⁴
- **October 5: FDA orders postmarket surveillance studies.** The manufacturers must answer whether their instructions are sufficient to ensure user adherence, the percent of scopes that remain contaminated after proper reprocessing, and the factors that contribute to contamination and what is needed to fully decontaminate the device.¹³⁵
- **November 13: FDA issues a mandatory recall of Custom Ultrasonics AERs.** FDA

warned that Custom Ultrasonics AERs may not reliably clean devices and recommended that the hospitals and health facilities using about 2,800 Custom Ultrasonics machines move as quickly as possible to a different manufacturer's AERs.¹³⁶

- **December 31: FDA issues draft “emerging signals” guidance.** FDA's new guidance explains the agency will now notify the public when it learns about potentially serious device issues rather than wait until the agency has reached a conclusion about a problem or formed recommendations.¹³⁷

While FDA has taken a number of actions to address the outbreaks in 2015, the inability to access information about adverse events independently from hospitals and manufacturers, and the inability to query data in electronic health records and claims data, stymied FDA's investigation and response to the spreading superbug infections and other dangerous illnesses.

Overall, FDA had major gaps in information, or delays in receiving information, which led to an unacceptably slow response to the spread of deadly infections in ERCP patients. While some of the responsibility for this failure lies with the agency for losing a key adverse event report and missing relevant international adverse event reports, without a more robust surveillance system independent from the reporting of manufacturers and hospitals, it is likely that the same gaps and delays will occur in other device related investigations.

FDA Needs a More Robust Device Safety Surveillance System

A passive device surveillance system is ineffective even when manufacturers and hospitals self-report information about device safety to FDA.

Even if device manufacturers and hospitals had worked to fulfill their regulatory obligations and provide FDA with the information they knew about device issues as rapidly and completely as

possible, FDA's passive device surveillance system probably would have still taken an unacceptably long time to identify the extent of the device issues. Assuming an MDR is filed and contains relevant information, staff reviewers can assess the seriousness of a particular incident, but are unlikely to make connections or see patterns because MDRs are not linked to the reports of similar devices from the same or other manufacturers with the same type of adverse event. Even in the unlikely event that a staff member sees a sufficient number of reports related to particular device to notice a pattern, FDA reviewers lack a denominator of the total number of times a device is used, and accordingly, have no way of assessing how frequent or serious issues are relative to how often a device is used. If a reviewer sees ten MDRs reporting a device failure, it is almost impossible to know if that is ten out of 100 procedures, ten out of 10,000 procedures, or ten out of one million.

The current system provides no ability to run data analytics to help identify patterns or to alert FDA to unusual types of reports. The system as it is currently designed allows FDA only to query the passive database to pull up all the information it has about a specific device. This is only useful, however, once FDA suspects there is a problem and specifically runs a search related to

that issue. Even so, FDA queries do not always pull up all the relevant information. Spelling mistakes and differences in the way that devices are named make searches difficult, and prior to February 2014, FDA relied on paper rather than electronic submissions.¹³⁸ Occasionally, as in the case of the initial Olympus UPMC MDR, paper adverse event reports received by the agency have been lost.

In contrast to the outdated and ineffective post-market monitoring system for devices, FDA has moved towards a more modern and effective system for overseeing the postmarket safety and effectiveness of drugs. The Food and Drug Amendments Act of 2007 (FDAAA) required FDA to establish a surveillance system that uses electronic health care data to monitor drugs using the unique product identifier known as an NDC, which is also included on all pharmacy insurance claims and on Medicaid claims for outpatient drugs prescriptions.¹³⁹ In 2009, FDA began to leverage the data provided by NDCs through the “Sentinel” initiative, which queries multiple health care data sources, including electronic health records and insurance claims information, to make links between patient outcomes and specific drugs.¹⁴⁰ The NDCs provide the key to making that link.

A system like Sentinel for devices is critical for two primary reasons. First, it does not rely exclusively on hospitals or manufacturers to report adverse events against weighty competing interests, but rather pulls information directly from databases that contain real-time information from insurance claims and other data that tracks patient care.¹⁴¹ This reduces the reliance on hospitals and manufacturers to self-report which, as this investigation has revealed, can happen months or even years after the fact and often lack important information. Second, Sentinel provides FDA with a “denominator” so that FDA can understand the number of adverse incidents reported in the context of the total number of patients treated.

Although it is not yet fully developed, a pilot “mini-Sentinel” has already substantially improved FDA’s postmarket surveillance of drugs. For example, after being alerted to cases of serious intestinal issues linked to the blood pressure drug Olmesartan, FDA analyzed the data in Sentinel to assess whether such issues were limited to the particular drug or whether all similar drugs caused intestinal problems.¹⁴² FDA was able to determine that only Olmesartan was linked to higher rates of celiac disease, and therefore notify patients of particular issues with a specific drug rather than

an entire class of drugs.¹⁴³ Similarly, after receiving a large number of reports of fatal bleeding associated with the drug Dabigatran to treat abnormal heart rhythms, FDA used the information in Sentinel to assess whether the rates of bleeding in Dabigatran patients were in fact higher than the rates in the clinical trial.¹⁴⁴ FDA found that the rates were not significantly different from the results of the trial or from other similar drugs on the market, which ensured that doctors knew they could safely continue prescribing Dabigatran.¹⁴⁵

A Sentinel-like system can also assist FDA and manufacturers to complete postmarket surveillance studies of the safety or effectiveness of a device required under section 522 of the Food, Drug, and Cosmetic Act (section 522 postmarket surveillance studies). Currently, there are few incentives for clinicians and patients to participate in the studies, and without UDI codes in claims data, it is difficult for device manufacturers to find ways to link use of their devices to patient outcomes.¹⁴⁶ A Sentinel system would help manufacturers to run more accurate studies quickly to answer lingering questions around the safety of duodenoscopy and AER design. Moreover, a Sentinel system would allow FDA to run its own queries and investigations without relying on manufacturers, who have few incentives to complete the studies quickly.

Currently FDA cannot use Sentinel or similar system to perform surveillance on devices because there is no similar way to track specific devices across different health claims databases. The Food and Drug Administration Amendments Act of 2007 required FDA to issue regulations to create a UDI system for medical devices.¹⁴⁷ Like the NDCs for drugs, UDIs will be placed on medical device labels and packages. FDA issued the final rule in September of 2013 which phases in the UDI requirements over time starting in September 2014 and ending in September of 2020.¹⁴⁸

UDIs will be required to be included on MDR reports, which should make it easier for FDA to query its system to identify reports linked to particular devices.¹⁴⁹ The UDIs, however, unlike NDCs, are not currently included on insurance claims.¹⁵⁰

A system like Sentinel for surveillance of devices could have prevented life-threatening infections worldwide.

In September 2013, when FDA first started investigating the design of duodenoscopes, outbreaks of CRE potentially linked to closed-channel devices had occurred at Thomas Jefferson Hospital, Virginia Mason, Carolinas Medical Center, and Froedtert Hospital but had not yet been reported to federal regulators by device manufacturers or hospitals. If FDA had access to UDIs in insurance claims, it is possible that the agency could have identified those outbreaks for itself at the beginning of its investigation and potentially moved faster to understand that the design of duodenoscopes makes them difficult or impossible to reliably clean, developed consensus internally about the source of the problems, and more promptly taken action to warn patients and hospitals.

Instead, after learning about the reprocessing problems at Advocate Lutheran from CDC, FDA took more than 17 months to issue its first safety alert to hospitals and almost two years to provide hospitals with additional measures to supplement their reprocessing of duodenoscopes. In the intervening months, at least 68 patients in the United States and 82 patients worldwide were infected with superbug and other antibiotic-resistant bacteria. Those infections, along with other infections that likely occurred but were never identified, could possibly have been prevented if

68 patient infections in the United States may have been prevented if hospitals had been alerted by FDA earlier to reprocessing difficulties.

hospitals been aware of the reprocessing difficulties known to FDA a year and a half before its first safety warning about the devices.

In the case of duodenoscopes, FDA was overly cautious and waited to alert the public and hospitals to the risks posed by duodenoscopes until the agency had finished its investigation and developed recommendations for supplemental reprocessing procedures. FDA's release of draft guidance on December 31, 2015, which explains that the agency will now notify the public about emerging serious device issues more quickly, is a positive step that will allow the agency, the public, and hospitals to take action sooner when new device issues arise.

The inability to access adequate information about adverse events independently from hospitals and manufacturers, and the inability to gather information about devices from insurance claims data, stymied FDA's investigation and expedient attention and response to the spreading antibiotic-resistant infections and other dangerous illness.

Overall, major gaps or delays in receiving information led to an unacceptably slow response from

the FDA to the spread of deadly infections in ERCP patients. Without a more robust surveillance system independent from the self-interested reporting of manufacturers and hospitals, it is likely the same gaps and delays will continue to occur with other device related investigations.

Conclusion

Senator Murray's staff investigation demonstrates that duodenoscopes spread life-threatening superbug and other antibiotic-resistant infections among patients in a number of hospitals throughout the United States and Europe in 2013 and 2014. These outbreaks occurred despite the fact that the manufacturer of 85 percent of the duodenoscopes used in the United States, Olympus, was aware by early 2012 that its closed-channel duodenoscope could harbor dangerous bacteria even after repeated and careful cleaning according to instructions.

Multiple hospitals were also aware that duodenoscopes were linked to superbug and other antibiotic-resistant infections in ERCP patients. Yet none of the three manufacturers of duodenoscopes sold in the United States – Olympus, Fujifilm, and Pentax – and only one hospital, ever alerted CDC to the infections. The device manufacturers and most hospitals also largely failed to meet their legal obligations to provide complete and timely information about serious patient infections and deaths to manufacturers and/or FDA.

The duodenoscope manufacturers and Custom Ultrasonics, the manufacturer of an AER used to clean duodenoscopes between uses, failed at every level to meet basic expectations of transparency and openness and to actively engage with FDA to address contamination issues. This disregard for the spirit, and sometimes the letter, of the law resulted in potentially preventable serious and potentially fatal illnesses in hospitals around the world.

As a result, when FDA first became aware of the outbreak at Advocate Lutheran, the agency lacked critical pieces of information that would have better allowed its staff to understand the frequency with which infections were occurring and that duodenoscopes could remain contaminated even after reprocessing instructions were followed correctly. Throughout 2014, FDA investigated the infections but did not issue any safety communications to inform hospitals of the risk posed by even duodenoscopes that are reprocessed according to manufacturers' instructions and reprocessed with cleared AERs. While FDA took significant steps in 2015 to alert hospitals to the risks of

contaminated duodenoscopes, study supplemental cleaning procedures to help ensure the devices are safe for reuse, require new data from manufacturers to prove that their cleaning instructions work, recall about 2,800 AERs, and require manufacturers to conduct postmarket surveillance studies, these steps ought to have been taken months or even a year sooner.

This investigation clearly demonstrates the inability of FDA's current device surveillance system to accurately identify the extent of device problems when they occur, which poses an unacceptable risk to patients. In contrast to the surveillance system for drugs, which increasingly uses unique identifiers to track drug performance through electronic health records and insurance claims, the

In contrast to the surveillance
system for drugs, the device
surveillance system relies

device surveillance system continues to rely almost exclusively on the self-reporting and self-regulation of manufacturers and hospitals. Had FDA been able to utilize a similar surveillance system to pull information about ERCP patient outcomes from insurance claims

almost exclusively on the self-reporting of manufacturers and hospitals.

and health records data, it is possible that as early as September 2013 the agency would have understood the extent of the threat posed by contaminated closed-channel duodenoscopes. FDA would have been able to

identify outbreaks in far more facilities than were identified at the time and link those infections to particular models of duodenoscopes and AERs. As a result, the agency could have completed its investigation sooner and more quickly issued safety alerts to hospitals.

The failure of FDA's device surveillance system to rapidly identify and respond to duodenoscope-related superbug and antibiotic-resistant infections serves as just one example of the fallacy of a system that is primarily reliant on hospitals and device manufacturers to self-report information to FDA. This investigation has shown that the expectation for device manufacturers and hospitals, despite strong competing priorities, to file 501(k) applications for device modifications, adequately validate devices before they are marketed, and quickly and accurately report potential device-related injuries and deaths as required by the current system, is ineffective.

The systematic failures identified in this report are, unfortunately, likely not confined solely to duodenoscopes. Without improved communication for each stakeholder from hospitals to manufacturers to state and local health departments, to FDA and CDC, and without a comprehensive postmarket device surveillance system that supplements self-reporting from hospitals and manufacturers, future device-related safety issues are likely to go undetected for far too long and with life-threatening consequences.

Recommendations

In order to address the issues raised by this investigation, the HELP Committee minority staff recommends the following legislative and regulatory changes:

Recommendation #1: Congress should require and promote that unique device identifiers (UDIs) be included in insurance claims, electronic health records, and device registries.

The investigation demonstrates that FDA's reliance on self-reporting of adverse events by manufacturers and hospitals is unworkable and outdated, particularly when contrasted with the active postmarket surveillance system for drugs. The widespread inclusion of UDIs in medical

data including claims data, electronic health records, and registries, is an absolutely essential piece of any fully functional, high-quality device surveillance system. Without widespread adoption of UDIs in claims and electronic health data, FDA is severely hampered in its ability to move forward to implement an improved device surveillance system. Congress should require that claims data include the UDI number associated with medical devices used in procedures in order to ensure FDA is not caught in the dark when the next medical device is linked to serious illness, injury, or death.

Recommendation #2: FDA should evaluate whether modifications to the design of closed-channel duodenoscope are necessary to prevent the spread of infection, and if so, require manufacturers to rapidly implement any repairs through a phased recall to ensure that devices used by hospitals are safe for reuse.

This investigation has suggested that closed-channel duodenoscopes may spread infection between

uses even when manufacturers' instructions are followed correctly and an effective AER is used. At least three independent evaluators have found that potential design flaws with the Olympus closed-channel duodenoscope prevent hospitals from reliably cleaning the devices between procedures. FDA should thoroughly evaluate the design of closed-channel duodenoscopes and consider immediate implementation of a phased recall to make any repairs or modifications necessary to ensure effective reprocessing.

Recommendation #3: FDA should update its guidance to clarify when manufacturers are required to submit a notification to FDA for 510(k) clearance before marketing modified devices.

In 2011, after becoming concerned about the number of manufacturers that failed to submit a notification to FDA for 510(k) clearance to account for substantial device modifications, FDA promulgated new draft guidance to clarify the existing 1997 document, to update the instructions, and to accommodate new technological advances. That guidance was subsequently withdrawn at the instruction of Congress in the Food Drug Administration Safety and Innovation Act (FDASIA) of 2012. The investigation provides renewed evidence of the need for updated guidance for device modifications.

Consistent with FDASIA, FDA should issue updated guidance that clarifies important terms that may confuse manufacturers regarding whether a 510(k) clearance is required, and that makes clear that manufacturers should verify and validate any determinations that safety and effectiveness are not impacted by a device modification.

Recommendation #4: FDA should move faster to provide information to health care providers when the agency becomes aware of information suggesting that patient safety might be compromised by a medical device.

A key finding of the investigation is that it took FDA almost 18 months from the time they learned of duodenoscope-linked infections to issue a safety communication alerting hospitals and the public to the risk posed by closed-channel duodenoscopes. Had FDA promptly notified hospitals earlier that there were potential safety issues with the reprocessing of closed-channel duodenoscopes, additional cleaning measure could have been adopted more quickly and issues with AER machines may have been identified more rapidly. Overall, earlier communication might

have prevented dozens of life-threatening infections including some that have never been identified.

The HELP Committee minority staff are pleased to note that on December 31 2015, FDA issued draft guidance to update the agency's procedures for notifying the public about potential device safety issues.¹⁵¹ Rather than wait until the agency has finishes an investigation and reaches a conclusion, FDA will now alert the public about to emerging safety concerns when the agency receives new information about serious or widespread public health issues.

Recommendation #5: FDA should have clear authority to deny a 510(k) submission based upon insufficient reprocessing validation data.

The investigation conclusively demonstrates that relying on reusable device manufacturers to attest

that their reprocessing instructions have been sufficiently tested and will work reliably in real-world conditions is insufficient. FDA guidance issued in March 2015, "Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling guidance for Industry and Food and Drug Administration Staff," provides additional clarity that reprocessing data should be included with 510(k) submissions for some reusable devices. In order to ensure that manufacturers submit all the requisite validation data when marketing a new or modified device, Congress should clarify in statute FDA's authority to consider a 510(k) submission incomplete and deny marketing clearance if a reusable device manufacturer fails to provide validation data with the 510(k) submission.

Recommendation #6: Compliance with MDR reporting requirements should be a Condition of Participation in Medicare.

The investigation demonstrates that hospitals that performed exemplary public health work to identify and halt duodenoscope-linked antibiotic-resistant infections often failed to share that information with device manufacturers and to collaborate effectively with federal regulators. Hospitals that wish to participate in Medicare must meet certain conditions of participation specified and laid out in statute and regulation, including certain requirements for infection control and medical records services. In addition to enforcement efforts by FDA, Centers for Medicare and Medicaid Services should require that compliance with relevant medical device reporting requirements be included as a condition of participation in Medicare to ensure that state survey agencies and accrediting bodies such as the Joint Commission on Hospital Accreditation specifically examine whether hospitals are filing timely required medical device reports with hospitals or FDA.

Recommendation #7: Congress should fully fund a National Medical Device Evaluation System (NMEDS).

Widespread adoption of UDIs is an important step but is just one of many parts of a complete and robust device evaluation system. FDA must also facilitate a coordinating center to ensure interoperability between data sources and a governance structure to operate the system. Congress should provide sufficient funds for the agency to move towards these goals as rapidly as possible.

¹ Kristen Wnedorf, et.al, "Endoscopic Retrograde Cholangiopancreatography-Associated AmpC *Escherichia coli* Outbreak," *Infection Control & Hospital Epidemiology*, (March 30, 2015).

² *Id.*

³ FDA, Effective Reprocessing of Endoscopes used in Endoscopic Retrograde Cholangiopancreatography (ERCP) Procedures, Executive Summary 14 (2015),

www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/Gastroenterology-UrologyDevicesPanel/UCM445592.pdf [hereinafter FDA Executive Summary].

⁴ Press Release, CDC, Action Needed Now to Halt Spread of Deadly Bacteria (2013), www.cdc.gov/media/releases/2013/p0305_deadly_bacteria.html.

⁵ Documents show discrepancies in the number of patients reported and the date of the infections. An additional five patients may have been infected with a multidrug-resistant infection after ERCP procedures at UMPC in

summer and fall 2013 that were not reported to FDA.

⁶ Only six of these infections were linked to an Olympus duodenoscope. The remaining infections were linked to an unknown manufacturer's device.

⁷ FDA Executive Summary at 14.

⁸ *Id.* at 9.

⁹ *Id.* at 24; Letter from Keiichi Nagata, Division President, FUJIFILM Medical Systems USA, to Senator Patty Murray (June 19, 2015) (on file with the HELP Committee).

¹⁰ FDA Executive Summary at 24-25.

¹¹ FDA Executive Summary at 17-18.

¹² FDA, Center for Devices and Radiological Health, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling: Guidance for Industry and Food and Drug Administration Staff 5-6 (March 7, 2015), www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM253010.pdf.

¹³ *Id.*

¹⁴ *Id.* at 10.

¹⁵ FDA Executive Summary at 32-40.

¹⁶ FDA, "Classify Your Medical Device,"

www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=876.1500.

¹⁷ 21 C.F.R. § 876.1500.

¹⁸ A device is substantially equivalent to another device if it (1) has the same intended use and the same technological characteristics, or (2) has the same intended use but with different technological characteristics that (a) do not raise new questions of safety and effectiveness and (b) demonstrate that it is at least as safe and effective as the legally marketed device. *See* FDA, Premarket Notification 510(k), "What is Substantial Equivalence?", www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/PremarketSubmissions/PremarketNotification510k/#se.

¹⁹ *See* 21 C.F.R. § 807.

²⁰ *See* FDA, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling: Guidance for Industry and Food and Drug Administration Staff (March 17, 2015), www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM253010.pdf.

²¹ *Id.*; 21 C.F.R. 820.75.

²² *See* FDA, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling: Guidance for Industry and Food and Drug Administration Staff (March 17, 2015), www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM253010.pdf.

²³ 21 C.F.R. Section 803.50(a).

²⁴ 21 C.F.R. Section 803.30(a).

²⁵ FDA, "MedSun: Medical Product Safety Network,"

www.fda.gov/MedicalDevices/Safety/MedSunMedicalProductSafetyNetwork/default.htm?source=govdelivery.

²⁶ FDA Executive Summary at 11.

²⁷ As of Aug. 13, 2015, manufacturers and importers have been required to submit all MDRS electronically which should address some of these issues. (Medical Device Reporting: Electronic Submission Requirements, 79 Fed. Reg. 8832 – 8855).

²⁸ FDA, Draft Guidance for Industry and Food and Drug Administration Staff - Postmarket Surveillance Under Section 522 of the Federal Food, Drug and Cosmetic Act (Aug. 16, 2011), www.fda.gov/RegulatoryInformation/Guidances/ucm268064.htm.

²⁹ The Brookings Institution, "Strengthening Patient Care: Building an Effective National Medical Device Surveillance System," 12 (Feb. 2015), www.brookings.edu/~media/research/files/papers/2015/02/23-medical-device-policy-surveillance/med-device-report-web.pdf

³⁰ *Id.*

- ³¹ Josh Rising, Ian Reynolds, and Art Sedrakyan, Pew Charitable Trusts, “Delays and Difficulties in Assessing Metal-on-Metal Hip Implants” (July 6, 2012), www.pewtrusts.org/en/about/news-room/opinion/2012/07/16/delays-and-difficulties-in-assessing-metalonmetal-hip-implants.
- ³² FDA, “FDA’s Sentinel Initiative- Background,” www.fda.gov/Safety/FDAsSentinelInitiative/ucm149340.htm.
- ³³ 21 U.S.C. § 360(i); Unique Device Identification System 78 Fed. Reg. 58786 – 58828.
- ³⁴ See FDA Executive Summary at 9.
- ³⁵ *Id.* at 25-27. The closed-channel duodenoscope models include the Olympus TJF-Q180V, the Fujifilm ED-530XT, and the Pentax ED-3490TK and ED-3670TK.
- ³⁶ MDR 8010047-2012-00157.
- ³⁷ Dr. Ir. Arjo Loeve, Delft University of Technology, “Investigation Olympus TJF-Q180V scope: Following detected contamination after cleaning and disinfection” (May 15, 2012) [hereinafter Delft report].
- ³⁸ Telephone conversation with Dr. Arjo Loeve (October 2, 2015).
- ³⁹ Delft report at 11.
- ⁴⁰ *Id.* at 23-24.
- ⁴¹ *Id.* at 23.
- ⁴² *Id.*
- ⁴³ *Id.* at 23-24.
- ⁴⁴ Delft report at 23-24.
- ⁴⁵ *Id.*
- ⁴⁶ *Id.*
- ⁴⁷ A. Bruijn, A. Drogelen., National Institute for Public Health and the Environment Ministry of Health, Welfare, and Sport, “Disinfection of Olympus TFJ-Q180V ERCP endoscope” (July 30, 2013) [hereinafter RIVM report].
- ⁴⁸ *Id.* at 1.
- ⁴⁹ *Id.* at p. 6.
- ⁵⁰ See, e.g., MDR 8010047-2015-00216.
- ⁵¹ Telephone conversation with staff at UPMC (October 29, 2015).
- ⁵² MDR 8010047-2012-00481.
- ⁵³ Letter from Scott Lucas, Program Manager at ECRI Institute to William Schaffner, Senior Associate Counsel at UPMC (December 26, 2012) (on file with the HELP Committee).
- ⁵⁴ MDR 8010047-2012-00481; Memorandum from Mary Ann Drosnock to David Barlow, Simon Nguyen, Laura Storms-Tyler, and Mia Zhang (December 14, 2012) (on file with the HELP Committee); Letter from Scott Lucas, Program Manager at ECRI Institute to William Schaffner, Senior Associate Counsel at UPMC (December 26, 2012) (on file with the HELP Committee).
- ⁵⁵ Letter from Scott Lucas, Program Manager at ECRI Institute to William Schaffner, Senior Associate Counsel at UPMC (December 26, 2012) (on file with the HELP Committee).
- ⁵⁶ Telephone conversation with staff at UPMC (October 29, 2015).
- ⁵⁷ Olympus has provided documentation that confirms the MDR was sent to FDA.

- ⁵⁸ Biotech Germande study 2128.Oly.2012 (: 08-Jan-2013) (on file with the HELP Committee).
- ⁵⁹ Biotech Germande study 2231.Oly.2013 (July 2, 2014) (on file with the HELP Committee).
- ⁶⁰ Bonn University studies on file with the HELP Committee. It is unclear whether the scope evaluated by Bonn University was linked to a particular outbreak
- ⁶¹ Letter from Olympus to customers, “Important Safety Advice” (Jan. 2013), www.swissmedic.ch/recalllists_dl/07207/Vk_20130123_15-e1.pdf (emphasis added).
- ⁶² These three outbreaks are: Erasmus Medical Center in the Netherlands, UPMC in the United States, and Clinique de Bercy in France.
- ⁶³ Letter from Olympus to customers, “URGENT: Field Safety Corrective Action” (2014,

www.swissmedic.ch/recalllists_d/10220/Vk_20140729_02-e1.pdf (emphasis added).

64 These ten outbreaks are: Erasmus Medical Center, UPMC, Clinique de Bercy (two outbreaks), Evangelisches

Waldkrankenhaus Spandu, Hartford Hospital, Froedtert Hospital, NYP/Weill Cornell Medical Center, UMass Memorial Hospital, and Charite-Universitätsmedizin,

⁶⁵ See 21 C.F.R 807.81(a)(3).

⁶⁶ FDA, “Deciding When to Submit a 510(k) for a Change to an Existing Device. Memorandum # K97-1” (1997), www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm.

⁶⁷ *Id.*

⁶⁸ Letter from LaShonda M. Long, Chief of Surveillance and Enforcement Branch I, to Laura Storms-Tyler, Vice President of Olympus Medical Systems Corporation, “It Has Come to Our Attention” (March 18, 2014),

www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM436587.pdf.

⁶⁹ See 21 C.F.R. § 820.30(g).

⁷⁰ See 21 C.F.R. 820.75; FDA Executive Summary at 30.

71 FDA, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling, Guidance for Industry and Food and Drug Administration Staff, 22-23 (2015),

www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf

⁷² RIVM report at p. 9.

⁷³ *Id.* at p. 4.

⁷⁴ *Id.* at ps. 7-8.

⁷⁵ In March 2015 FDA found that Olympus had validated updated reprocessing instructions. FDA, Safety Communication “Olympus Validates New Reprocessing Instructions for Model TJF-Q180V Duodenoscopes” (March 26, 2015), www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm439999.htm.

⁷⁶ FDA, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling, Guidance for Industry and Food and Drug Administration Staff (March 17, 2015), www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf

⁷⁷ Hospitals and other user facilities are required to report serious injuries linked to devices to manufacturers but are not required to report serious injuries to FDA.

⁷⁸ MDR 8010047-2012-000157 (understating the number of patients infected at Erasmus Medical Center).

⁷⁹ See, e.g., MDR 8010047-2013-00595 (Clinique de Bercy) (“improper reprocessing could not be ruled out as a contributory factor”); MDR 8020047-2013-00092 (Charite-Universitätsmedizin); MDR 8010047-2012-000452 (Clinique de Bercy).

⁸⁰ Letter from Jan B. Welch, Acting Director, Office of Compliance, FDA, to Akihiro Okubo, President, Olympus Medical Systems Corporation, “Warning Letter” (Aug. 12, 2015), www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm458510.htm.

⁸¹ Letter from Keiichi Nagata, Division President FUJIFILM Medical Systems USA to Senator Patty Murray (June 19, 2015) (on file with the HELP Committee).

⁸² Letter from Anastacia M. Bilek, Director, Division of Premarket and Labeling Compliance, FDA, to Mr. Teiichi Goto, Corporate Vice President, Fujifilm Corporation, “It has come to our attention” (Aug. 12, 2015), www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM458552.pdf.

83 *Id.*

⁸⁴ Letter from Anastacia M. Bilek, Director, Division of Premarket and Labeling Compliance, to Mr. Hiroshi Suzuki, President and CEO, Hoya Corporation (PENTAX Life Care Division), “It has come to our attention” (Aug. 12, 2015), www.fda.gov/downloads/MedicalDevices/ResourcesforYou/Industry/UCM458554.pdf.

⁸⁵ FDA, Form 483, Observation 1, inspection of a Fujifilm Facility in Ashigarakami Gun, Japan (April 23-May 01, 2015).

86 *Id.*

87 *Id.*

⁸⁸ *Id.* (observation 3).

⁸⁹ Letter from Jan B. Welch, Acting Director, Office of Compliance, FDA to Mr. Hiroshi Suzuki, President and

- CEO, Hoya Corporation (PENTAX Life Care Division), Warning Letter (Aug 12, 2015), www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm458487.htm.
- ⁹⁰ Pentax instructs user facilities to use either an EtO/Carbon Dioxide 80:20 or 90:10 mixture when sterilizing a duodenoscope but the validation was performed with an EtO/HCFC 10:90 gas mixture – a different mixture from the gas included on the label. (*Id.*).
- ⁹¹ FDA, Safety Communication, “FUJIFILM Medical Systems, U.S.A., Inc. Validates Revised Reprocessing Instructions for Model ED-530XT Duodenoscopes” (Dec. 23, 2015), www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm439999.htm
- ⁹² Letter from Jan B. Welch, Acting Director, Office of Compliance, FDA to Mr. Hiroshi Suzuki, President and CEO, Hoya Corporation (PENTAX Life Care Division), Warning Letter (Aug 12, 2015), www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm458487.htm.
- ⁹³ Letter from Jan B. Welch, Acting Director, Office of Compliance, FDA to Mr. Teiichi Goto, Corporate Vice President, Fujifilm Corporation, Warning Letter (Aug. 12, 2015), www.fda.gov/iceci/enforcementactions/warningletters/2015/ucm458453.htm.
- ⁹⁴ In November, 2014 Pentax reported patients at a hospital in Udine, Italy developed a *Klebsiella pneumoniae* infection after undergoing ERCP. MDR 9610877-2015-00046.
- ⁹⁵ Email from counsel to Pentax to HELP committee staff (October 28, 201) (on file with the HELP Committee).
- ⁹⁶ Letter from Counsel for Fujifilm to Senator Patty Murray (October 2, 2015) (on file with the HELP Committee).
- ⁹⁷ Press Release, FDA, “FDA orders recall under consent decree for all custom ultrasonics automated endoscope reprocessors” (Nov. 13, 2015), www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm472605.htm.
- ⁹⁸ Letter from Thomas D. Gardine, District Director, FDA, to Frank J. Weber, President & CEO, Custom Ultrasonics, Warning Letter (June 22, 2005), [/www.fda.gov/ICECI/EnforcementActions/WarningLetters/2005/ucm075455.htm](http://www.fda.gov/ICECI/EnforcementActions/WarningLetters/2005/ucm075455.htm).
- ⁹⁹ FDA, Safety Communication, “Custom Ultrasonics, Inc. Endoscope Washer/Disinfectors” (Feb. 27, 2007), www.fda.gov/MedicalDevices/Safety/AlertsandNotices/PublicHealthNotifications/ucm064361.htm.
- ¹⁰⁰ Telephone conversation with FDA (Dec.7, 2015).
- ¹⁰¹ Letter from Anne E. Johnson, Acting Director, Philadelphia District, Office of Regulatory Compliance and Capt. Sean Boyd, Acting Director of Compliance, FDA, to Alicia Nakonetschny, President and CEO, Custom Ultrasonics (Nov. 12, 2015), www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHFOIAElectronicReadingRoom/UCM472567.pdf.
- ¹⁰² *Id.*
- ¹⁰³ 21 C.F.R. § 803.30.
- ¹⁰⁴ *Id.*
- ¹⁰⁵ Committee staff were unable to obtain information from Carolinas Medical Center in Charlotte North Carolina after repeated inquiries.
- ¹⁰⁶ For state reporting requirements *see* Association for Professionals in Infection Control and Epidemiology, “Summary of State CRE Reporting Requirements,” www.apic.org/Resource/_TinyMceFileManager/Advocacy-PDFs/CRE_ReportingRequirements_Final.pdf.
- ¹⁰⁷ Telephone conversation with staff at Virginia Mason (October 29, 2015).
- ¹⁰⁸ *Id.*

- ¹⁰⁹ MDR 2951238-2014-00644.
- ¹¹⁰ MDR 2518897-2015-00329.
- ¹¹¹ 21 C.F.R. § 803.30(a)(1).
- ¹¹² Letter from Thomas Kraus, Associate Commissioner for Legislation, FDA, to Senator Patty Murray (May 14, 2015) (on file with the HELP Committee).
- ¹¹³ MedWatch 5029305.
- ¹¹⁴ MedWatch 5032234.

¹¹⁵ Telephone Call with staff at Virginia Mason (October 29, 2015).
¹¹⁶ There is no federal requirement that user facilities report all antibiotic-resistant infections, or even all CRE outbreaks, to the CDC. Instead, hospitals voluntarily report hospital-acquired infections to the National Healthcare Safety Network (NHSN) or the Gram-Negative Bacilli Surveillance Initiative (MuGSI). MuGSI was created specifically to track CRE infections but includes data from only eight surveillance sites in Colorado, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee. The CDC has been unable to confirm that any of the identified outbreaks prior to fall 2013 were reported to any of their databases. See CDC, “What is NHSN?” (last accessed Nov. 30, 2015), www.cdc.gov/nhsn/about-nhsn/index.html; CDC, “Technical Information-Multi-Site Gram-Negative Bacilli Surveillance Initiative (MuGSI)” (last accessed Nov. 30, 2015), www.cdc.gov/hai/eip/mugsi_techinfo.html.
¹¹⁷ 21 C.F.R. § 803.30 (emphasis added).
¹¹⁸ FDA Executive Summary at 11.
¹¹⁹ Telephone conversation with staff at Advocate Lutheran (November 19, 2015).
¹²⁰ *Id.*
¹²¹ MDR 8010047-2012-00157. There were actually at least 30 patients infected.
¹²² MDR 8010047-2012-00481. Olympus has provided supporting documentation that the original report was sent to FDA, but it does not appear that it was ever entered into FDA’s adverse event reporting database and FDA experts conducting the investigation do not appear to have seen this MDR until a later time.
¹²³ MDR 2951238-2013-00031.
¹²⁴ MDR 8010047-2012-00452.
¹²⁵ MDR 8010047-2013-00092.
¹²⁶ MDR 8010047-2013-00176.
¹²⁷ MW 5031083.
¹²⁸ Letter from Senator Patty Murray to Margaret Hamburg, FDA Commissioner (February 3, 2014), www.murray.senate.gov/public/_cache/files/096ecf61-0004-4076-b2e0-8fd4f1a25e78/020315-virginia-mason-letter.pdf.
¹²⁹ FDA, Safety Communication, “Design of Endoscopic Retrograde Cholangiopancreatography (ERCP) Duodenoscopes May Impede Effective Cleaning” (February 19, 2015 updated March 4, 2015), www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm434871.htm.
¹³⁰ CDC, “Interim Duodenoscope Surveillance Protocol,” www.cdc.gov/hai/organisms/cre/cre-duodenoscope-surveillance-protocol.html.
¹³¹ FDA, Reprocessing Medical Devices in Health Care Settings: Validation Methods and Labeling, Guidance for Industry and Food and Drug Administration Staff (March 17, 2015), www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm253010.pdf.
¹³² FDA Executive Summary. Virginia Mason has extensively studied the culture and quarantine protocol at its facility, and continues to find about two percent of its duodenoscopes remain contaminated after reprocessing even using Olympus’s updated cleaning instructions.
¹³³ FDA, Safety Communication, “Supplemental Measures to Enhance Duodenoscope Reprocessing” (Aug. 4, 2015), www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm454766.htm.
¹³⁴ Letter from Jan B. Welch, Acting Director, Office of Compliance, FDA to Mr. Teiichi Goto, Corporate Vice President, Fujifilm Corporation, Warning Letter (Aug. 12, 2015), www.fda.gov/iceci/enforcementactions/warningletters/2015/ucm458453.htm; Letter from Jan B. Welch, Acting

Director, Office of Compliance, FDA to Mr. Hiroshi Suzuki, President and CEO, Hoya Corporation (PENTAX Life Care Division), Warning Letter (Aug 12, 2015), www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm458487.htm; Letter from Jan B. Welch, Acting Director, Office of Compliance, FDA, to Akihiro Okubo, President, Olympus Medical Systems Corporation, “Warning Letter” (Aug. 12, 2015), www.fda.gov/ICECI/EnforcementActions/WarningLetters/2015/ucm458510.htm.
¹³⁵ Press Release, FDA, “FDA orders duodenoscope manufacturers to conduct postmarket surveillance studies in health care facilities” (Oct. 5, 2015), www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm465639.htm.

¹³⁶ Press Release, FDA, “FDA orders recall under consent decree for all custom ultrasonics automated endoscope reproprocessors, (Nov. 13, 2015), www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm472605.htm.

¹³⁷ Public Notification of Emerging Postmarket Medical Device Signals (“Emerging Signals”); Draft Guidance, 80 Fed. Reg. 81829 – 81830.

¹³⁸ FDA published a final rule on February 13, 2014 requiring manufacturers and importers to submit electronic MDRs in a reviewable format, but allowed for hardcopy submissions until August 13, 2015. User facilities are allowed to continue submitting hardcopy MDRs but are given the option of e-filing reports as well. Medical Device Reporting: Electronic Submission Requirements, 79 Fed. Reg. 8832 – 8855.

¹³⁹ See Deficit Reduction Act of 2005 § 6002; 42 U.S.C. § 1396r-8(a); 21 U.S.C. § 360; Drug Listing Act of 1972, §§ 3, 4.

¹⁴⁰ FDA, “Sentinel Program Interim Assessment (FY 15)” (Sept. 24, 2015), www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM464043.pdf.

¹⁴¹ *Id.* at 12.

¹⁴² *Id.* at 23-24.

¹⁴³ *Id.* at 23-24.

¹⁴⁴ *Id.* at 21-22.

¹⁴⁵ *Id.*

¹⁴⁶ See Brookings Institution, Strengthening Patient Care: Building an Effective National Medical Device Surveillance System (Feb. 2015), www.brookings.edu/~media/research/files/papers/2015/02/23-medical-device-policy-surveillance/med-device-report-web.pdf.

¹⁴⁷ Food and Drug Administration Amendments Act of 2007 § 226; 21 U.S.C. § 360i(f).

¹⁴⁸ Unique Device Identification System 78 Fed. Reg. 58786 – 58828.

¹⁴⁹ “Medical Device Reporting” 21 C.F.R. §§ 803.32-33, 803.42, 803.52.

¹⁵⁰ The Office of the National Coordinator for Health Information Technology’s “2015 Edition Health Information Technology Certification Criteria” rule made progress towards enabling access to and sharing of unique device identifier information. This rule requires that federally-certified health information technology allow a user to access a list of UDIs for a patient’s implantable devices and share it with other authorized users. 80 Fed. Reg. 62601.

Appendix I: Letters

The following are reproductions of the letters Senator Murray sent to Olympus, Pentax, Fujifilm, and FDA.

Appendix II: Reports

This appendix includes a report of the results of Dr. Arjo

Loeve's investigation of the TJF-Q180V closed channel duodenoscope involved in the outbreak of antibiotic-resistant infections at Erasmus Medical Center in the Netherlands. It also includes the report of the Dutch National Institute for Public Health and the Environment (RIVM) investigation into the design and safety of the TJF-Q180V duodenoscope and the response of Erasmus Medical Center. The translation of this report from the original Dutch to English is not endorsed or verified by RIVM.

Investigation Olympus TJF-Q180V

Scope detected contamination after cleaning and disinfection

(Internal title: Report Investigation Scope G-206)

Reporting, Conclusions and Recommendation

May 15, 2012

Final Version - Revision June 27, 2012 – Adding external title August 29, 2014

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1 Background - Contamination 'Scope G-206'

Recently the bacterium *Pseudomonas Aeruginosa* was found at the Erasmus Medical Center ('Erasmus MC') in the cavity of the tip of an Olympus video duodenoscope TJF-Q180V (hereinafter referred to as 'Scope G-206', where the number 206 refers to the internal registration number of the related scope within the Erasmus MC). This bacterium persisted after manual cleansing and mechanical cleaning and disinfection in the Olympus ETD3 scope disinfectant.

In order to locate the cause of the persistence of the detected bacteria, it was decided to extensively inspect Scope G-206, to take samples at places that are normally within reach. It will then step by step disassembled and inspected. Sampling will be taken in areas that have become accessible through the disassembly. Also due to these sampling-and disassembling steps and the subsequent microbiological and viral investigations (hereinafter referred to as 'the investigation'), it is attempted to discover if the persistence of the bacteria is caused by:

- Incorrect or insufficient following of the cleaning instructions
- Incorrect or insufficient formulated cleaning instructions
- Insufficient functioning of sealing in Scope G-206
- Other cause(s)

Olympus Nederland and the Erasmus MC have decided together to take care of and to carry out a further investigation of the contamination of Scope G-206. On April 23, 2012 an investigation team (hereinafter referred to as 'the investigation team'), consisting of representatives of the Erasmus MC and Olympus, as well as an independent expert of the Delft University of Technology ('TU Delft'), has conducted the investigation at Olympus Nederland B.V., Industrieweg 44, Zoeterwoude, Netherlands.

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2 Purpose and layout of this report

Purpose of this report is to come to an [objective determination of the cause / causes of the persistence of the Pseudomonas Aeruginosa bacterium in Scope G-206](#).

For this purpose, first a factual record (supported by photos as well as registration and result lists) of the briefing and execution of the investigation is provided.

Following the findings during the Investigation, the independent expert of the TU Delft has formulated an opinion concerning the most likely cause / causes of the persistence of the Pseudomonas Aeruginosa bacterium in Scope G-206.

In this report, the sample reference numbers are given as {0000}

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3 Disclaimer

Photo used in this report were taken by a professional photographer. The photos were corrected visually regarding color to compensate for deviations by changing light sources and using different cameras. (Overview and macro photos were made with a Nikon D300s and microscope photos with the connected camera). Colors may therefore still differ slightly from the actual colors as they would have been observed under daylight or under daylight lamps. Due to differences in color rendering by different monitors, printers or kinds of paper, possible deviations could be stronger.

Conclusions regarding observations should in no way be based on shades of color or specific characteristic, absolute color values based on the utilized photos.

The conclusions, estimations and recommendations as shown in Chapter 6 "Opinion of the independent expert" are conclusions, estimations en recommendations based on the observed facts during the investigation, the know-how and experience of the independent expert (Arjo Loeve, see Chapter 4) and confidential discussions between the independent expert, experienced fellow scientists and Head of the Department Prof. Dr. Jenny Dankelman in the Biomechanical Engineering Department of the Delft University of Technology, Faculty 3ME.

Therefore conclusions, estimations en recommendations in Chapter 6 can be seen as an informed expert opinion, but in no way a formal position of the Delft University of Technology.

The names used to refer to parts of the scope in this report are not necessarily the same as names commonly used or names used within Olympus. For example: A 'sealing' can also be known as 'bonding' or a 'cap' can be referred to as 'cover'/'sleeve'/'housing'. In this report, consistent and unambiguous use of names was taken care of as much as possible.

In case of uncertainty or doubt about which part is identified by a particular name, you will need to contact the author before drawing conclusions and / or take consequences regarding this report.

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4 Briefing Report

The investigation was conducted on April 23, 2012 at Olympus Nederland B.V., Industrieweg 44, Zoeterwoude.

At around 10:15 hrs., the investigation team gathered there consisting of:

Name	Job Function	Organization		
Henk Braat	Managing Director	Olympus	Nederland	B.V.
Knut Burmester	Section Manager Service Engineering	Olympus Europa Holding GMBH		
Viktor Tran	Production Support Specialist MSD	Olympus Europa Holding GMBH		
Kees Verdouw	Service Engineer Flexible Instruments	Olympus	Nederland	B.V.
Marcel Vonk	Sales Support Manager CDS Unit Head	Olympus	Nederland	B.V.
Leo Abel	Gastroenterology & Liver Diseases Dept.	Erasmus	Medical	Center
Jolanda Buijs-Hegeman	Staff Advisor Medical Devices	Erasmus	Medical	Center
Leo Groenendaal	Unit head of Medical Technology	Erasmus	Medical	Center
Johan de Kat	Hospital Hygienist	Erasmus	Medical	Center
Annelies Poth	Expert Medical Devices Hospital	Erasmus	Medical	Center
Annette Sandijck	Hygienist	Erasmus Medical Center		
Arjo Loeve	Researcher Biomechanical Engineering	Delft University of Technology		

A number of issues relating to the people present are specifically addressed:

- Henk Braat leading the meeting indicates that he will not be present during the investigation.
- Arjo Loeve as an independent expert from the TU Delft will take care of reporting, photo / video shooting for recording, and will observe the process objectively and critically and will manage when necessary.
- Leo Abel will take care of the sampling and will wear latex gloves.
- Viktor Tran takes care of the scope disassembly and will wear latex gloves.
- Annette Sandijk takes care of the storage of the sample materials.
- Johan de Kat will take care of the labeling and packaging of the samples.
- Kees Verdouw will provide and operate any auxiliary equipment such as microscopes.

It is discussed what the approach during the investigation will be:

- 1 Sampling working channels and tip of Scope G-206 with a 3mm diameter cytology brush in order to determine possible presence of residual patient material. Only those samples will be taken in the clean room and attendees present will be wearing gloves and masks.
- 2 Step-by-step disassembling of Scope G-206. For each disassembly step, the relevant part of the scope will be visually inspected, photographed and sampled with cytology brushes and / or swabs. Components of Scope G-206 would also partially or completely be packed for further investigation (cultures, NACT PCR and viral).
- 3 At a later stage components of Scope G-206 will be examined with an electron microscope in order to determine the presence of possible biofilms.

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- 11:23 hrs. Preparing the work tables (disinfecting and covering them with a sterile cloth). Those present in the clean room are wearing protective coats and surgical masks. Leo Abel samples the scope and wears in addition to the protective coat and the surgical mask, also sterile gloves and a surgical cap.
- 11:31 hrs. Sampling for PCR in a clean room. Present in the clean room are: Leo Abel, Arjo Loeve, Annelies Poth, Annette Sandijck, Marcel Vonk. The rest of the investigation team observes from a technical location.
- Sampling the parts below with sterile 3 mm diameter cytology brushes (after sampling by brushing and/or pigging, each brush is collected in a new and sterile laboratory jar):
 - Air/water channel and instrument channel tip {5379} (Figure 1).
-

Figure 1: Tip of Scope G-206 and the cytology brush used.

-
- The cavity under the forceps elevator ("behind the forceps elevator" according to the sample list) {5388} (Figure 2). It should be noted that it was impossible to reach behind/below the forceps elevator cytology brushes since these have a hard tip. Grooves, holes and cracks in that part of the tip could not be reached
-

Figure 2: Sampling of the cavity under the forceps elevator.

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-
- Biopsy / instrumentation channel {5396} and biopsy port {5401} (Figure 3).
-

Figure 3: Sampling biopsy channel (above and left middle) and biopsy port (right middle and below).

11:40 hrs.	The investigation team is located in the technical area. The rest of the investigation will take place there. It was decided that the Scope G-206 or parts exposed between the disassembly steps do not need to be cleaned due to the low probability of relevant cross-contamination (since the search is focused on a very specific bacterium).
11:43 hrs.	Viktor makes the first cut in the sealant of cardan rubber, directly behind the steerable tip of the scope and observes air bubbles in the sealing. He suspects that the sealant was applied by a third party. Further investigation shows that Erasmus MC does not use a third party for repairs; this sealant was applied by Olympus Nederland B.V.. Arjo requests to pause in order to first take photos of the coating, Figure 4. The scope is moved to the microscope in order to take photos of the tip.

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Figure 4: Cutting the sealant of cardan rubber open and microscope photos of the air bubbles (some of them are open) in the still untouched parts of the sealing. The air bubbles are indicated with arrows.

Photos of the camera and light source in the tip show:

- brownish scale **behind** the cover glass of the camera (Figure 5)
 - cracks in the sealing of the housing of the tip around the camera (Figure 5)
-

Figure 5: Visual inspection camera housing. On the left and right, it is clearly visible that the scale is located behind the glass covering of the camera. On the right, a vertical arrow points to the tear in de sealing of the housing. Furthermore, on the right another tear can be seen in de sealing of the camera which is indicated with the diagonal arrow.

Photos of the cavity in which the forceps elevator moves, made with the microscope and a small diameter fiberscope, show (Figure 6 en 7):

- scratches and grooves reaching under the forceps elevator,
 - whitish scale in the tip housing and also brownish scale on the metal part where the forceps elevator runs {5412, 5423, 5434}.
-

Figure 6: Visual inspection of the tip around the forceps elevator. Above: scratches and grooves well below the forceps elevator; the arrows point to the scratches. Below: whitish and brownish scale (arrow) on the surface where along the forceps elevator moves.

Figure 7: From left to right: sampling of the space around the forceps elevator with swab; scraping sample of white and brown scale; overview of work setting, cutting of scalpel point for packaging.

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12:22 hrs. Viktor Viktor removes the sealing with which the hard plastic cap of the cardan part of the scope is connected. This sealing is packaged as sample {5445}. Then under the adhesion on the flexible sleeve which covers the steerable part will take place using a swab {5456, 5467} (Figure 8).

Figure 8: Removing and packaging of the sealant between the hard plastic cap of the tip and the cardan rubber of the scope and (far right) sampling under the cardan rubber.

Viktor removes the hard plastic cap from the tip by cutting it open and prying it loose from the adhesive layer that glues it to the metal interior of the tip. Waste from cutting the cap is packaged for further testing {5478} (Figure 9). Then sampling with swabs took place inside the housing on which the hard plastic cover was glued {5489, 5490} (Figure 9).

Figure 9: (First two photos on the left) Cutting open and prying loose of the hard plastic cap on the tip. (Two photos on the right) Sampling interior under the removed hard plastic cap.

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It was attempted twice to reach behind the forceps elevator with a swab for sampling. However, the limited space does not lend itself for a deep sampling. Therefore superficial sampling at the rear end of the forceps elevator took place as well as in the forceps elevator channel {5507, 5516} (Figure 10). Another attempt was made to sample deep behind the forceps elevator using a cytology brush. This was a bit more successful, but the space was still too limited for the brush to reach behind the forceps elevator {5521} (Figure 10).

Figure 10: Sampling behind the forceps elevator with swabs and cytology brush.

Inspection of the forceps elevator hinge under the microscope (Figure 11) showed that the hinge has relatively speaking a lot of room to maneuver. When the forceps elevator was moved, a fiber catapulted from this hinge. This fiber was picked up with the point of a scalpel and packaged for further investigation {5535}.

Figure 11: Microscope images of the forceps elevator hinge and the fiber that emerged from it. The axial shifting of the forceps elevator due to room for maneuvering is clearly visible in the two photos. Arrows point to the location of the fiber

12:56 hrs.

LUNCH BREAK. All participants leave the technical area and continue with the investigation only after Arjo was present again.

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13:27 hrs. **CONTINUATION.** Het investigation team is present again in the technical area. Viktor removes the cover plate that covers de actuator area of the forceps elevator (Figure 12, left). The cover plate is packaged for further testing {5609}. Then the propulsion cable of the forceps elevator is sampled twice with swabs {5542, 5558} (Figure 12, right). What is immediately noticeable is the fact that all metal surfaces inside the opened actuator area are covered in brown scale. Further testing is needed to determine if this is the result of oxidation or something else.

Figure 12: (Left) Verwijdering afdekplaat (rechter pijl) van actuator area forceps elevator (linker pijl). (Right) Sampling propulsion cable forceps elevator.

Two swab samples were taken from the deep area in which the lever of the forceps elevator moves back and forth {5560, 5573} (Figure 13, first three on the left). After disconnecting and pushing aside the propulsion cable of the forceps elevator (using a precision screwdriver), the area where the propulsion cable was originally running on was sampled twice with swabs {5584, 5599} (Figure 13, far right).

Figure 13: (First three photos on the left) Sampling of the deep area in which the lever of the forceps elevator moves back and forth. (Far right) Sampling under the propulsion cable of the forceps elevator.

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13:54 hrs.

Viktor removes the glue from the screw which mounts the forceps elevator on the axis of the lever, lifting axle. The screw is removed and packaged for further testing {5677}. The lever with lifting axle forms one single part which is lifted from the actuator area and put under the microscope (Figure 14). There is an O-ring around the lifting axle that should create a watertight separation between the actuator area and the patient.

Lever

O-ring Lifting Axle

*Figure 14: From left to right: lifting away of the lever with lifting axle; actuator area from where the lever was removed; lever with lifting axle and O-ring photographed from the side that was in the actuator area; lever with lifting axle and O-ring photographed from the side of the lifting axle.
The O-ring was mounted on the forceps elevator.*

In the far right photo in Figure 14, it can be clearly seen that all surfaces of the lever and lifting axle that were located in the actuator area, the actuator area-side, was covered with brown scale. The lifting axle looks clean at the side where the forceps elevator (and therefore also the patient) was located, the patient-side.

Under the microscope, the lever is sampled twice with swabs at the actuator area-side {5613, 5620} and twice on the lifting axle that was located in the forceps elevator {5636, 5648} (Figure 15).

Figure 15: Lever with lifting axle and O-ring (dark blue arrow) and the forceps elevator (white arrow).

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Under the microscope the difference between the brown-scaled actuator-side area and the clean-looking patient-side of the lever with lifting axle is clearly visible again (Figure 16). The O-ring shows signs of wear and is on the actuator-side area heavily covered with brown scale. On the surface of the O-ring (where it is wedged in the housing) the brown scale is also prominently present. On the patient-side of the O-ring is the brown scale still present, but to a lesser extent.

Actuator housing-side

Patient-side

Patient-side
Patient-side

Actuator housing-side

Patient-side

Actuator housing-side

Figure 16: Microscope images of the lever with lifting axle and O-ring. In each of the bottom four photos, there is an enlargement of the central part of the photo on the left.

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Viktor removes de O-ring from the lifting axle. The O-ring is cut into two halves, both of them are packaged for further testing {5651, 5664} (Figure 17). The forceps elevator and the lever with lifting axle are also packaged for further testing {5682, 5695}. Finally, a virological sample is taken from the water suction channel {5706} before the tip of Scope G-206 is packaged with a sterile bag and the scope in is stored in its case (Figure 17).

Figure 17: From left to right: removing the O-ring; cutting the O-ring in half; virological sample from water suction channel; packaging of Scope G-206.

14:23

Since Viktor and Knut must catch their plane back to Germany, the investigation is terminated. Therefore it is refrained from sampling of the inside of the scope shaft, the removal and cutting up of the working channel for further testing, and the sampling of the inside of the handle of Scope G-206.

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6. Opinion independent expert

Accessibility for brushes

Observations: During the sampling it became repeatedly clear that the tip of Scope G-206 contains several cracks, corners and spaces that are hard to reach or cannot be reached at all with the 3 mm diameter cytology brush. In particular:

- the crack under the hinge point of the forceps elevator,
- the crack caused by the axial clearance of the forceps elevator,
- and the area under/behind the curve of the forceps elevator,

proved unreachable for this brush (Figures 2, 10 and 11).

Recommendation: Enlarge in the scope design the space around the mentioned points so that these can be reached by brushes and / or make sure that the cleaning instructions are such that those points are cleaned thoroughly in the current scope in one way or another. Validate that the customized designs and / or instructions actually result in sound cleaning.

Quality of sealing

Observations: The sealing in and around the tip were found to show abnormalities that could result in potential leakage. Specific observations:

- air bubbles, some of them open, in the adhesion between the hard plastic cap of the tip and the flexible sleeve over the steerable part of the scope (Figure 4),
- cracks in the sealing around the camera housing (Figure 5),
- Worn looking O-ring which should ensure the sealing around the lifting axle (Figure 12).

The air bubbles in the adhesion and the tear in the sealing can open the door for the appearance of moisture and micro-organisms. Visualization of the O-ring with a scanning electron microscope. Based on the images of the O-ring, in particular the rough / powdery texture of the surface and the crack that can be seen in the electron microscope photo (see Appendix B), it appears that reliable sealing by means of

this O-ring cannot be not guaranteed. This is further supported by the findings as described below under 'Scale found on parts'.

Recommendation: Ensuring regular, strict control of sealing between moments of use. Take care of regular replacement of the O-ring (it might have performed well over time, but it remains a moving sealing which requires maintenance). Improve in future scope designs the sealing by creating multiple barriers or, and this would be preferred, avoid such sealing at all and design a forceps elevator with no moving parts that run from the patient into a "sterile" area of the instrument.

Scale on parts

Observations: At a number of locations in the tip of Scope G-206, scale was detected:

- brownish scale behind the glass covering of the camera (Figure 5),
- brownish and whitish scale on the edge of the space around the forceps elevator (Figure 6),
- brownish scale on the surfaces in de actuator area (Figure 12),
- brownish scale on the surfaces of the lever at the actuator area-side (Figure 16),
- brownish scale on the O-ring, mainly at the actuator area-side, but also at the patient-side (Figure 16).

Scale behind the covering glass of the camera implies that this area was not properly sealed, so that growth of micro-organisms, scale from residual liquids or deterioration of a possible coating occurred.

Scale on the edge of the area around the forceps elevator should be investigated further before arriving at any conclusions. This could be oxidation, but in case of a contamination it could also indicate insufficient / incorrect cleaning by the Erasmus MC, since this location is well and easily accessible.

The brownish scale on the surfaces in de actuator area, the actuator area-side of the lever and the O- ring is so consistent and evenly distributed that it is highly unlikely that this oxidation is caused by, for example, skin contact during assembling. It is more likely that somewhere from the shaft or the tip of the endoscope moisture and / or biological material has entered the actuator area and lingered and / or augmented.

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The fact that the brownish scale of the O-ring can be seen on each side of the O-ring (area actuator-side and patient-side) suggests that this scale around and on the O-ring has migrated from one side to the other. It is therefore very likely that this O-ring has not done its job. Furthermore, it appears that also the size of the cracks between the forceps elevator and the housing as well as between the lifting axle and the housing are too small to be able to be brushed (and perhaps also to be rinsed) and too large to be inaccessible for liquids and / or biological materials.

Experience with O-ring-sealing on this scale shows that less than 0.01mm deviation from the ideal clearance can already cause leakage. More scale could therefore increase the chance of leakage or scale can be caused by leakage. During the axial back and forth movement of the lifting axle, the O-ring could make axially rolling movements, which could cause moisture and / or organic material to enter between the O-ring and the lifting axle. With each further movement of the lifting axle, moisture and / or organic material could migrate further from the actuator housing- side to the patient-side or vice versa.

Recommendation: Find out what the scale behind the glass covering of the camera is, measure the quality of the sealing and correct when necessary. Review the cleaning process critically in order to trace how the scale in the forceps elevator channel on an easily accessible location could linger and stay unnoticed.

Improve the sealing of the actuator area or avoid in future designs the use of such sealing. Check the existing sealing in all existing scopes and ensure an objective, critical, quantitative measuring of the sealing quality.

Cultures

Observations: Culture results are shown in Appendix A, Table A.2. Only the cultures (specific as well as generic) of the hard plastic cap of the tip provided positive culture results. Since the exterior of the cap has been cleaned repeatedly, can be accessed easily, has been dry for a long time, (the detected bacterium normally does not thrive on dry surfaces), it is therefore highly likely that the bacterium was located on the inside of the cap. This finding also fits the observations made regarding the quality of the sealing.

The fact that there were no positive culture results at other points does not mean that none were there. The inaccessibility of many places on the tip, the limitations of the sampling with swabs and the fact that biofilms grow more easily on plastics and rubbers than on metals, result in the fact that little can be concluded based on the negative test results.

Recommendation: Also make a culture of the spare sample of the O-ring {5651}. If possible, conduct a detailed investigation to exclude the presence of unwanted biomaterials in the actuator area. Since apparently *Pseudomonas Aeruginosa* was found inside the tip, it seems prudent to investigate immediately all scopes worldwide of a similar type. See also recommendations in the 'Quality of Sealing' and in the 'Conclusion' sections.

Conclusion

Observations: All in all, it seems that this scope has suffered badly from usage, possible insufficient quality of sealing, inadequate maintenance and lack of critical mechanical control. The very small cracks and spaces in the forceps elevator channel form a number of locations where lingering and / or increasing moisture and / or biological materials are quite likely.

It goes without saying that the sealing, actuator area en O-ring require direct and serious attention in all existing and future scopes similar to Scope G-206.

Recommendation: Increase direct global control and maintenance of similar scopes, revise especially scopes with degraded sealing, and conduct extensive sampling. Update the cleaning instructions and conduct strict controls to ensure compliance and acceptable results. Improve the quality of the sealing in the scope design and minimize the amount of sealing points.

In case during further testing *Pseudomonas Aeruginosa* or other bacteria/viruses/substances are also found that should not be present in the actuator area, it is recommended to immediately recall all similar scopes and/or in parallel to investigate if there could (also) be a leakage trail that does not run via the O-ring or other sealing.

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Appendix A – Registration numbers and descriptions of cultures
Scope G-206

Table A.1: Sample material and locations and relating reference numbers.

Material / Location	Reference number
Air/water channel tip	5379
Behind forceps elevator	5388
Biopsy channel	5396
Biopsy port	5401
Contamination tip, top	5412
Scalpel 1	5423
Scrapings after scalpel 1	5434
Adhesion cap	5445
Swab under adhesion 1	5456
Swab under adhesion 2	5467

Cap	5478
Culture without cap 1	5489
Culture without cap 2	5490
Under forceps elevator after removing cap 1	5507
Under forceps elevator after removing cap 2	5516
Brush under forceps elevator without cap	5521
Scalpel with fiber	5535
Cable forceps elevator tip 1	5542
Cable forceps elevator tip 2	5558
Housing forceps elevator channel for O-ring 1	5560
Housing forceps elevator channel for O-ring 2	5573
Sample under cable in tip 1	5584
Sample under cable in tip 2	5599
Cover plate forceps elevator operating housing	5609
Operating forceps elevator patient side 1	5613
Operating forceps elevator patient side 2	5620
Operating forceps elevator instrument side 1	5636
Operating forceps elevator instrument side 2	5648
Half of O-ring 1	5651
Half of O-ring 2	5664
Screw backside forceps elevator	5677
Forceps elevator	5682
Lever	5695
Water suction channel (virological sample)	5706

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Reference number	Lab Number	Type	Date	Result
5379	Handed to Annelies Poth for DNA Investigation			
5388	Handed to Annelies Poth for DNA Investigation			
5396	Handed to Annelies Poth for DNA Investigation			
5401	Handed to Annelies Poth for DNA Investigation			
5412	20120072678101	AERK	2012-04-	negative
5423	20120072674701	AERK	2012-04-	negative
5434	20120072680001	AERK	2012-04-	negative
5445	20120072666701	VIM	2012-04-	negative

5456	20120072681901 AERK	2012-04- negative
5467	20120072683501 VIM	2012-04- negative
5478	20120072675501 VIM	2012-04- VIM pseu, B-DYK-9760
5478	20120072677101 AERK	2012-04- E. Faecium, B-DYK-9757
5478	20120072677101 AERK	2012-04- VIM pseu, B-DYK-9756
5489	20120072686101 AERK	2012-04- negative
5490	20120072688601 VIM	2012-04- negative
5507	20120072689401 AERK	2012-04- negative
5516	20120072695801 VIM	2012-04- negative
5521	Handed to Annelies Poth for DNA Investigation	
5535	20120072673901 AERK	2012-04- negative
5542	20120072700201 AERK	2012-04- negative
5558	20120072705301 VIM	2012-04- negative
5560	20120072711701 AERK	2012-04- negative
5573	20120072717601 VIM	2012-04- negative
5584	20120072729901 AERK	2012-04- negative
5599	20120072734401 VIM	2012-04- negative
5609	Spare for possible future cultures and / or counter-expertise	
5613	20120072737901 AERK	2012-04- negative
5620	20120072740801 VIM	2012-04- negative
5636	20120072745901 AERK	2012-04- negative
5648	20120072750401 VIM	2012-04- negative
5651	Spare for possible future cultures and / or counter-expertise	
5664	Handed to Annelies Poth for DNA Investigation	
5677	Electron microscopy	
5682	Electron microscopy	
5695	Electron microscopy	
5706	6159-E	CELK 2012-04- negative

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Appendix B - Electron microscope photos

The electron microscope photos in this appendix are made with a scanning electron microscope by the Vossius-institute in Leiden.

Figure B. 1: Photo of the O-ring which clearly shows that the surface of the O-ring is rough and fibrous, contains scale and was torn at the left bottom.

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Figure B.2: a few more enlargements of the surface of the O-ring.

Figure B.3: Photos of the surface from the bottom of the sealing between the hard plastic cap of the tip and the cardan rubber of the scope.

Appendix C - Contact sheets all photos of the investigation

p.30 - Investigation Scope 206

D300s-ACL0006-eKL.jpg

D300s-ACL0008-eKLsq.jpg

D300s-ACL0012-eKL.jpg

D300s-ACL14-eKL.jpg

D300s-ACL0017-eKL.jpg

D300s-ACL18-eKL.jpg

D300s-ACL22-eKL.jpg

D300s-ACL0023-eKL.jpg

D300s-ACL0027-eKL.jpg

D300s-ACL29-eKL.jpg

D300s-ACL0036-eKLsq.jpg

D300s-ACL0040-eKL.jpg

D300s-ACL0043-eKL.jpg

D300s-ACL0045-eKL.jpg

D300s-ACL0052-eKLSq.jpg

D300s-ACL0053-eKL.jpg

D300s-ACL0057-eKL.jpg

D300s-ACL60-eKL.jpg

D300s-ACL0064-eKL.jpg

D300s-ACL65-eKL.jpg

D300s-ACL0069-eKL.jpg

D300s-ACL72-eKL.jpg

D300s-ACL0083-eKL.jpg

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D300s-ACL0131-eKLsq.jpg

D300s-ACL0135-eKL.jpg

D300s-ACL136-eKL.jpg

D300s-ACL140-eKL.jpg

D300s-ACL0141-eKL.jpg

Microsc-4.jpg

Microsc-12.jpg

Microsc-19.jpg

Microsc-020.jpg

Microsc-25.jpg

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Microsc-026.jpg

Appendix III: Communications from Olympus to Customers in Europe

The following are letters sent by Olympus to customers in Europe.

Appendix IV: Selected Adverse Event Reports

The following reports are copies of medical device reports and MedWatch reports sent by manufacturers and hospitals to FDA to account for incidents of antibiotic-resistant infections linked to ERCP procedures. This compilation is not inclusive of all device reports filed by manufacturers and hospitals but rather is meant to provide a sample of the reports for each outbreak of duodenoscope-linked infections between 2012 and spring 2015.

Advocate Good Samaritan Hospital Downers Grove, Illinois

Advocate Lutheran General Hospital
Park Ridge, Illinois

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MAUDE Adverse Event Report: PENTAX PENTAX PENTAX DUODENOSCOPE

510(k) 7	DeNovo 8	Registration & Listing 9	Adverse Events 10	Recalls 11	PMA 12	HDE 13	Classification 14	Standards 15
CFR Title 21 16	RadiationEmitting Products 17	XR ay Assembler 18	Medsun Reports 19	CLIA 20	TPLC 21	Inspections 22		

PENTAX PENTAX PENTAX DUODENOSCOPE

Back to Search Results

Model Number ED3490TK
Event Date 06/21/2013
Event Type Injury
Event Description
Pt underwent an ercp procedure using a pentax ed3490tk a110084 side viewing duodenoscope. Pt developed a cre infection. Proper cleaning of scope confirmed as per company recommendations. Organism found under elevator on scope.

[Search Alerts/Recalls](#)[23](#)

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Brand NamePENTAX
Type of DevicePENTAX DUODENOSCOPE
Manufacturer (Section D)PENTAX
3 Paragon Drive
Montvale NJ 07645
MDR Report Key3252445
Report NumberMW5031083
Device Sequence Number1
Product CodeFDT25
Report SourceVoluntary
Reporter OccupationRISK MANAGER
Type of ReportInitial
Report Date07/23/2013
/ Device Was Involved in the Event
/ Patient Was Involved in the Event
Date FDA Received07/23/2013
Is This An Adverse Event Report?No
Is This A Product Problem Report?Yes
Device OperatorHealth Professional
Device MODEL NumberED3490TK

Device LOT Number: A110084
 Was Device Available For Evaluation? Yes

Is The Reporter A Health Professional? No

Is this a Reprocessed and Reused Single Use Device? Yes

Patient TREATMENT DATA

Date Received: 07/23/2013 Patient Sequence Number: 1

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13. </scripts/cdrh/cfdocs/cfHDE/hde.cfm>
14. </scripts/cdrh/cfdocs/cfPCD/classification.cfm>
15. </scripts/cdrh/cfdocs/cfStandards/search.cfm>
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19. </scripts/cdrh/cfdocs/Medsun/searchReportText.cfm>
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21. </scripts/cdrh/cfdocs/cfTPLC/tplc.cfm>
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23. <http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/default.htm>
24. <https://www.accessdata.fda.gov/scripts/medwatch/>
25. [./cfPCD/classification.cfm?start_search=&ProductCode=FDT](/cfPCD/classification.cfm?start_search=&ProductCode=FDT)

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14. </scripts/cdrh/cfdocs/cfPCD/classification.cfm>
15. </scripts/cdrh/cfdocs/cfStandards/search.cfm>
16. </scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm>
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20. </scripts/cdrh/cfdocs/cfClia/Search.cfm>
21. </scripts/cdrh/cfdocs/cfTPLC/tplc.cfm>
22. </scripts/cdrh/cfdocs/cfTPLC/inspect.cfm>
23. <http://www.fda.gov/MedicalDevices/Safety/ListofRecalls/default.htm>
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Allegheny General Hospital Pittsburgh, Pennsylvania

Boca Raton Regional Hospital
Boca Raton, Florida

Carolinas Medical Center, Charlotte North Carolina

Cedars-Sinai Medical Center
Torrance, California

**Charite-Universitätsmedizin
Berlin, Germany**

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**Clinique De Bercy
Charenton-le-Pont, France**

**Erasmus Medical Center
Rotterdam, Netherlands**

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**Evangelisches Waldkrankenhaus Spandu
Berlin, Germany**

**Fox Chase Cancer Center,
Philadelphia, Pennsylvania**

**Froedtert Hospital
Milwaukee, Wisconsin**

Hartford Hospital
Hartford, Connecticut

**Massachusetts General Hospital,
Boston, Massachusetts**

New York-Presbyterian/Weill Cornell Medical Center
New York City, New York

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MAUDE Adverse Event Report: OLYMPUS OLYMPUS ERCP ENDOSCOPE

510(k)7	DeNovos8	Registration & Listing9	Adverse Events10	Recalls11	PMA12	HDE13	Classification14	Standards15
CFR Title	RadiationEmitting	XRays	Medsun	CLIA20	TPLC21	Inspections22		
2116	Products17	Assembler18	Reports19					

OLYMPUS OLYMPUS ERCP ENDOSCOPE

Back to Search Results

Model Number J180
Event Date 12/20/2012
Event Type Malfunction
Event Description

This pt and 15 subsequent pts developed klebsiella pneumoniae infections after having undergone endoscopic retrograde cholangiopancreatogram (ercp) procedures. The problem was thought to be related to difficulty in reliably cleaning and disinfecting the mechanically complex 'elevator' at the distal end of the endoscope. In response, the method of reprocessing was changed from automated highlevel disinfection (hld) to gas sterilization. In addition, all staff was retrained in scope precleaning, cleaning, and highlevel disinfection. The retraining and hdl was assessed by obtaining brush specimens of the elevator after hld of 10 ercp scopes that had been used on pts with known infection of the biliary tract. All of these cultures were negative.

Search Alerts/Recalls23

New Search | Submit an Adverse Event Report24

Brand NameOLYMPUS
Type of DeviceERCP ENDOSCOPE
Manufacturer (Section D)OLYMPUS

Center Valley PA 18034

MDR Report Key3413223

Report NumberMW5032234

Device Sequence Number1

Product CodeKOG25

Report SourceVoluntary

Reporter OccupationATTORNEY

Type of ReportInitial

Report Date10/09/2013

2 DeviceS WERE Involved in the Event:1 2

0 PatientS WERE Involved in the Event:

Date FDA Received10/10/2013

Is This An Adverse Event Report?No

Is This A Product Problem Report?Yes

Device OperatorHealth Professional

Device MODEL NumberJ180

Is The Reporter A Health Professional?No

Is this a Reprocessed and Reused SingleUse Device?No

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6. </scripts/cdrh/devicesatfda/index.cfm>
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MAUDE Adverse Event Report: OLYMPUS MEDICAL SYSTEM CORPORATION DUODENOVideoscope

510(k) De Novo	Registration & Listing	Adverse Events	Recalls	PMA	HDE	Classification	Standards
77 CFR Title	Radiation-Emitting	X-Ray	Medsun	CLIA	TPLC	Inspections	
21	Products	Assembler	Reports				
1616	1717	1818	1919				

OLYMPUS MEDICAL SYSTEM CORPORATION DUODENOVideoscope

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Lot Number N/A
Device Problem No Known Device Problem
Event Type Injury
Event Description

Olympus received a news article which reported that eight patients tested positive for carbapenem-resistant enterobacteriaceae (cre) infections after undergoing a procedure using a duodeno videoscope (model/serial number unspecified) at the user facility. In addition, it was stated the hospital cultured its scopes and found no bacteria matching the strain causing the patient's infections. The exact cause of the patient's outcome cannot be conclusively determined at this time. Originally, (b)(6) 2015 olympus was informed of one patient infection in which the patient was medically treated with antibiotics. Based on the new information received olympus will submit seven mdrs to account for the eight patients. (cross reference: 2951238-2015-00388, 2951238-2015-00389, 2951238-2015-00390, 2951238-2015-00391, 2951238-2015-00392, and 2951238-2015-00393) olympus followed up with the user facility to obtain additional information regarding the reported events by telephone and in writing but with no result.

The user facility has not provided the specific model and serial number of the scopes involved into the reported events. Therefore, it is unknown if the user facility has returned the scope to olympus for service or evaluation. As part of our investigation in this report, olympus dispatched an endoscopy support specialist (ess) to the user facility to observe their reprocessing practices. At this time the user facility has not yet scheduled a date for the in-service. If additional and significant information becomes available at a later time these reports will be supplemented please see original associated medical device report: 2951238-2015-00249.

[New Search²⁴](#) | [Submit an Adverse Event Report^{25,24}](#)

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Patient TREATMENT DATA
Date Received: 08/25/2015 Patient Sequence Number: 1

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MAUDE Adverse Event Report: OLYMPUS OLYMPUS 160/180 SERIES ENDOSCOPE ERCP
SCOPE 1160

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	CFR Title			Radiation-Emitting Products		X-Ray Assembler		Medsun Reports			[CLIA]	20	[TPLC]
	21	16		17		18		19			22		

OLYMPUS OLYMPUS 160/180 SERIES ENDOSCOPE ERCP SCOPE 1160

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Lot Number 2001160

Event Date 02/27/2013

Event Type Malfunction

Event Description

Over a 2 year period, there was an increase in the number of kp resistant microbiology (kpc) reported results. During investigation, it was determined that a small percentage of involved patients had undergone endoscopic procedures. Endoscopes were cultured by microbiology department. One endoscope tested positive for kpc following disinfection. The endoscope was removed from use. (b)(6) was consulted. A review of endoscope cleaning, disinfection and related processes was documented by (b)(6). Staff were interviewed, reprocessing documents reviewed, audits completed. The subject endoscope was tested by third party laboratory, (b)(4). Third

party laboratory culture results were negative for kpc. Investigation and analysis of kpc is ongoing and sources of kpc remains undetermined at this time. Official olympus report received, root cause unknown. Dates of use: (b)(6) 2011 - (b)(6) 2012.

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Brand NameOLYMPUS 160/180 SERIES ENDOSCOPE
Type of DeviceERCP SCOPE 1160
Manufacturer (Section D)OLYMPUS
2400 Ringwood Ave.
San Jose CA 95131
MDR Report Key2999629
Report NumberMW5029305
Device Sequence Number1
Product CodeFDS²⁵
Report SourceVoluntary
Reporter OccupationNurse
Type of ReportInitial
Report Date03/04/2013
I Device Was Involved in the Event
I Patient Was Involved in the Event
Date FDA Received03/04/2013
Is This An Adverse Event Report?No
Is This A Product Problem Report?Yes
Device OperatorHealth Professional
Device LOT Number2001160
OTHER Device ID NumberTJF-Q180V
Was Device Available For Evaluation?Device Returned To Manufacturer
Date Returned to Manufacturer01/08/2013
Is The Reporter A Health Professional?Yes
Is this a Reprocessed and Reused Single-Use Device?No

Patient TREATMENT DATA

Date Received: 03/04/2013 Patient Sequence Number: 1

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